CHAPTER 6

JMPR PRACTICES IN ESTIMATION OF MAXIMUM RESIDUE LEVELS, AND RESIDUES LEVELS FOR CALCULATION OF DIETARY INTAKE OF PESTICIDE RESIDUES

CONTENTS

6.1 INTRODUCTION

The JMPR evaluates the possible risks to consumers from pesticide residues in foods by assessing available residue data and then using this information to estimate the short-term and long-term dietary intakes of residues. This chapter deals with the residue data assessment and the following chapter will deal with estimating dietary intakes.

The following guidelines are provided for selecting data for estimation of maximum residue levels for establishing MRLs, and supervised trials median residue (STMR) levels as well as the highest residue in edible portion of composite sample (HR) where an acute reference dose (ARfD) had been established by the JMPR.

Maximum residue levels are estimated for residues in or on the portion of the commodities to which Codex MRLs apply. For dietary intake purposes the residue levels are estimated on the edible portion of the commodity. In some cases, however, sufficient data on the edible portion is not available. In this case, STMR and HR are also estimated on the commodities to which Codex MRLs apply.

In addition to residues in or on the whole commodity, the JMPR is also interested in residues in the edible part of the crop. Residues of systemic pesticides may be expected to be present in all parts of the crop, while residues of non-systemic pesticides are not always present or may be present in minor quantities in the edible part of a crop. For each pesticide, information on the distribution between edible and non-edible parts should be available to the JMPR from

supervised trials or specific experiments. This information is also essential for deciding on the toxicological acceptability of the dietary intake of residues on or in food commodities. For example, MRLs are established for whole bananas including the inedible peel. Some MRLs may appear to be unacceptably high, based on residues on the whole commodity. However, information that residues in the edible portion are practically non-detectable often alleviates that concern. Another example is oranges where usually most residues are found in the peel, especially for non-systemic pesticides.

Besides primary and some processed food commodities, when the available information permits, JMPR also recommends MRLs for animal feeds and food processing by-products, e.g., apple pomace and grape pomace, which can be used as animal feed and are traded internationally. With the exception of fresh forage commodities, animal feeds are commodities of trade and therefore require Codex MRLs if pesticide use results in detectable residues in the feed. While JMPR no longer recommends maximum residue levels for fresh forage commodities, residues in these animal feeds are taken into account when estimating livestock dietary burdens. Residues in feed may also lead to detectable residues in animal tissues, milk and eggs, necessitating MRLs for those commodities. Some food commodities themselves, e.g., cereal grains, may be used as feedstuffs for food-producing animals.

6.2 COMPARABILITY OF SUPERVISED TRIAL CONDITIONS TO GAP

General principles

When estimating maximum residue levels, the FAO Panel examines all residue data arising from supervised trials supporting or reflecting the reported GAPs. As a general precondition, for reliable estimation of maximum residue levels an adequate number of independent trials are required reflecting the highest of national maximum GAPs and conducted according to well designed protocols that consider geographical distribution and the inclusion of a number of different growing and management practices, and growing seasons.

Firstly, the uniformity or continuity of residue population reflecting GAPs is considered. When there is a large gap in residue values, indicated by a high coefficient of variation of residues in composite samples or other appropriate statistical methods, the presence of different populations may be suspected. In such cases the residue data and trial conditions need more stringent analysis before residue levels for MRL, STMR or HR can be estimated.

The decline rate of a pesticide may vary between different geographical locations due to such factors as the weather, cultivation practices and soil conditions. Under practical conditions the number of trials which can be performed for a given commodity is limited. Nevertheless, a larger data set *representing a statistically, not different residue population* provides a more accurate estimation of the selected percentile than a small data set derived from trials representing only one critical GAP. Consequently, where only limited number of trial data is available from a GAP, assumed to lead to the highest magnitude of residues, one approach is to consider those GAPs which may possibly lead to a similar magnitude of residues, and this assumption can be confirmed based on prior experience and with suitable statistical methods. However, caution must be exercised in combining residue data populations of statistically different magnitude, as it may lead to erroneous estimation of maximum residues, when based on statistical methods (described in the following section), and an underestimation of the dietary intake.

The JMPR takes into account the following general principles in selecting the residue data population(s) for the estimation of maximum residue levels, STMR and HR values.

Only the results of "supervised trials conducted at the highest nationally recommended, authorized or registered uses", i.e., maximum application rate, maximum number of treatments, minimum pre-harvest interval (PHI), are considered in estimation of maximum residue levels, i.e., maximum GAP per country.

If a sufficient number of trials are available, reflecting the maximum GAP of one country or geographical region, the MRL estimates should be based on those residue data alone.

Where prior experience indicate that the agricultural practice and climatic conditions lead to similar residues, the critical GAP of one country can be applied for the evaluation of supervised trials matching this critical GAP but carried out in another country.

The Meeting does not consider it appropriate to combine residue data sets deriving from different GAPs without sufficient justification. This method could include residue data with different median (mean) values, which would result in lower estimated daily intake and also lower MRLs if the latter would be calculated based on statistical methods, e.g., using the NAFTA statistical calculator.

When considering combining different residue data, the distribution of residue data is carefully examined and only those datasets combined which may be expected to arise from the same parent populations, based on comparable GAP. In such cases expert judgement can be assisted with appropriate statistical tests, e.g., Mann-Whitney U-test or Kruskal-Wallis H-test.

In establishing comparability of residue trials data in which more than one parameter, i.e., application rate, number of treatments or PHI, deviate from the maximum registered use, consideration should be given to the combination effect on the residue value which may lead to an underestimation or overestimation of the STMR. Generally, trials should not be used where two critical parameters of GAP deviate. For example, a trial result should not normally be selected for the estimation of the STMR if both the application rate is lower (perhaps 0.75 kg/ha in the trial; 1 kg ai/ha GAP) than the maximum rate registered and the PHI is longer (perhaps 18 days in the trial, 14 days GAP) than the minimum registered PHI, as these parameters could combine to underestimate the residue. When results are selected for the estimation of STMRs and HR values, despite combination effects, the reasoning should be outlined in the appraisal.

If a residue value is lower than another residue value from the same trial which is within GAP, then the higher residue value should be selected in identifying the STMR and HR values. For example, if the GAP specified a minimum PHI of 21 days and the residue levels in a trial reflecting GAP were 0.7, 0.6 and 0.9 mg/kg at 21, 28 and 35 days respectively, then the residue value of 0.9 mg/kg would be selected.

Application rate

The actual application rates in the trials should generally deviate no more than ±25% of the maximum application rate. Deviations from this should be explained in the appraisal.

Pre-harvest interval

The latitude of acceptable intervals around the PHI depends on the rate of decline of residues of the compound under evaluation. The allowable latitude should relate to a ±25% change in residue level and may be estimated from residue decline studies. As the rate of decline is gradually decreasing, the deviation corresponding to the +25% concentration is shorter than that reflecting the –25% concentration. The ranges around the label PHI for accepting supervised trials data are wider for a slowly declining residue than a rapidly declining residue.

The situation for 1st order decline is illustrated[26] in Figure 6.1. Where the information available does not enable applying this principle, the ±25% permissible deviation recommended by the OECD Guidelines may be applied, but it should be based on a case by case assessment, as in case of -25% PHI and rapidly declining residues it may lead to acceptance of larger residues than + 25%.

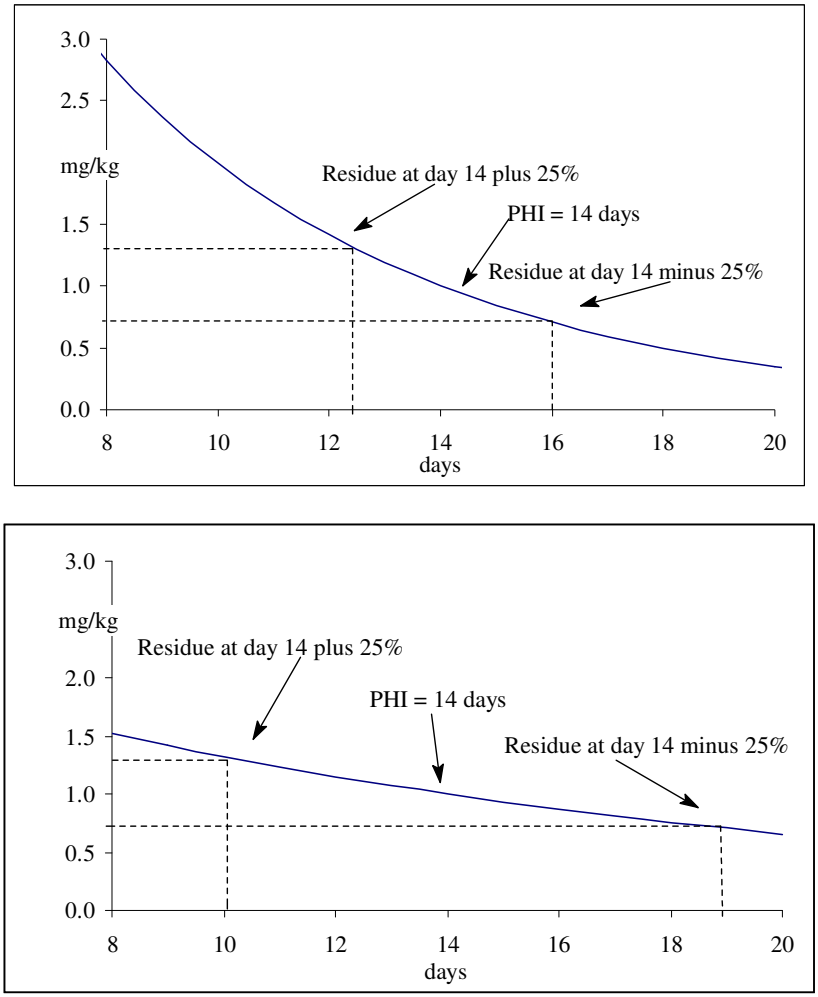

Figure 6.1 Illustration of latitude of permissible ± deviation from the PHI indicated on the label

For first order decay

$$C = C_0 \times e^{-kt} \quad \text{.....1}$$

At time t_1, $C_1 = C_0 \times e^{-kt_1}$

At time t_2, $C_2 = C_0 \times e^{-kt_2}$

$$\frac{C_1}{C_2} = e^{-k(t_1 - t_2)}$$

$$-k(t_1 - t_2) = \ln(\frac{C_1}{C_2}) \quad \text{.....2}$$

[26] Hamilton, D., Personal communication, 2009

Relation between k and $t_{1/2}$ (half-life)

$$\frac{C}{C_0} = 0.5 = e^{-kt_{1/2}}$$

$$\text{i.e.,} -k = \frac{\ln(0.5)}{t_{1/2}} \quad \text{.....3}$$

From 2 and 3

$$\frac{\ln(0.5)}{t_{1/2}} \times (t_1 - t_2) = \ln(\frac{C_1}{C_2})$$

$$\text{i.e.,}\ t_1 - t_2 = \ln(\frac{C_1}{C_2}) \times \frac{t_{1/2}}{\ln(0.5)} \quad \text{.....4}$$

If t_1 is the PHI and C_1 is the residue concentration at the PHI, we can calculate the time intervals where the concentration is within ± a chosen percentage.

C_2 = 125% of C_1	t_1-t_2 = 0.32 × $t_{1/2}$
C_2 = 75% of C_1	t_2-t_1 = 0.42 × $t_{1/2}$

When the PHI is more than a few days, the estimation of half-life should exclude the data from day 0 (day of application) because the initial decline of residues is generally much faster than the later decline. As the 1st order decline provided the best fit for about 35% of cases[27] of large number of trials, the calculation described with equations 1–4 may not always provide reliable estimates. However, the graphical method shown in Figure 6.1 can be used for any situation.

Number of treatments

Consideration of whether the number of applications reported in trials is comparable to the registered maximum number will depend on the persistence of the compound and the interval between applications. Nevertheless, when a large number of applications are made in trials (more than 5 or 6) earlier treatments should not be considered to contribute greatly to the final residue unless the compound is persistent or the treatments are made with unusually short intervals. Residue data are sometimes provided from just prior to the final treatment as well as after it, which is direct evidence of residue contributions from previous applications to the final residue. Also, treatments from more than about 3 half-lives (obtained from residue decline trials) prior to the final treatment should not make a significant contribution to the final residue.

Formulation

In many situations different formulations would cause no more variation than other factors, and data derived with different formulations would be considered comparable. The most common formulation types which are diluted in water prior to application include EC, WP, water dispersible granules (WG), suspension concentrates (SC) (also called flowable concentrates), and soluble concentrates (SL). Experience from trials demonstrates that these formulations lead to similar residues. Residue data may be translated among these formulation types for applications that are made to seeds, prior to crop emergence, i.e., pre-plant, at-plant, and pre-emergence applications, just after crop emergence or directed to the soil, such as row middle or post-directed applications (as opposed to foliar treatments).

[27] Timme, G.; Frehse, H., Laska, V. Statistical interpretation and graphic representation of the degradation behaviour of pesticide residues II. Pflanzenschutz-Nachrichten Bayer 33. 47-, Pflanzenschutz-Nachrichten Bayer, **1986**, 39, 187-203.

For late season foliar applications of formulations diluted in water, the decision on the need for additional data depends upon two factors: (1) the presence of organic solvents or oils in the product and (2) the pre-harvest interval. Provided the pre-harvest interval is longer than 7 days, formulations without organic solvents or oils will be considered equivalent for residue purposes. With the exception of water dispersible granular formulations, when the PHI is less than or equal to 7 days, bridging data will normally be needed to show residues are equivalent from these formulations.

For mid- to late-season uses of formulations containing organic solvents or oils, e.g., EC, or water in oil emulsions (EO), bridging studies should be provided to establish whether the residues resulted from their application are comparable to those obtained with another formulation.

6.2.1 Interpretation tables for supervised trials data

When residue data are available from several countries the results may be tabulated to show the comparison of trial conditions with GAP to assist with interpretation. In the example in Table XI.1 residue data on tomatoes from six countries are compared with GAP. Note that some countries specify application rate (kg ai/ha) while others specify spray concentration (kg ai/hL) in their GAP. Italian trials may be evaluated against the conditions of Spanish GAP.

This concept may also be used for tabulation of trial data used for evaluations of alternative GAP.

The interpretation table provides the set of residues that match maximum GAP from the various countries. The next step is to decide if the residues constitute a single population or different populations.

6.3 DEFINITION OF INDEPENDENT SUPERVISED RESIDUE TRIALS

The estimation of maximum residue level, STMR and HR values relies on the selection of residue data from trials within GAP. One data point (residue value) is selected from each relevant and independent trial. A sufficient number of trials are needed to represent field and cultural practice variability.

Judgements are needed on whether trials should be considered sufficiently independent to be treated separately.

The following trial conditions are usually recorded and are taken into consideration:

- geographical location and site – trials at different geographic locations are considered independent
- dates of planting (annual crops) and treatments - trials involving different planting dates or treatment dates are considered independent
- crop varieties – some varieties may be sufficiently different to influence the residue
- formulations – comparability or independence of trials with different formulations should to be assessed taking into account the principles described in sections **6**.2 and **6**.5
- application rates and spray concentrations – trials at significantly different application rates and spray concentrations are counted as separate trials;

- types of treatment, e.g., foliar, seed treatment, directed application – different types of treatment on different plots at the same site are considered as separate trials
- treatment operations – trials at the same site treated in the same spray operation are not counted as separate trials
- application equipment – trials at the same site treated by different equipment, other things being equal, are not counted as separate trials
- addition of surfactants – a trial with the addition of surfactant may constitute sufficient difference to be treated as independent.

As weather (not climate) is usually a major factor in determining the resultant residues for such trials, only one field trial would normally be selected per trial site if multiple plots/trials are conducted in parallel. For trials at the same location there should be convincing evidence that additional trials are providing further independent information on the influence of the range of farming practices on residue levels.

Various situations may apply when several residue values are described as "replicates" such as when there are:

a. replicate analysis samples from one laboratory sample (duplicate analysis)

b. replicate laboratory samples obtained with sub-division from one field sample

c. replicate field samples analysed separately (each sample is taken randomly through a whole sprayed plot)

d. replicate plots or sub or split-plot field samples are analysed separately (the whole trial is subject to the same spraying operation, but it is divided into 2 or more areas that are sampled separately)

e. replicate trial samples are analysed separately (trials from the same site that are not independent may be considered as replicate trials).

The reviewer should therefore specify the type of replicate when preparing the monograph.

The highest value of the residues from replicate field samples (c, d, e) should be taken as the single value for the trial, while the mean value of residues obtained from replicate test portions (a) withdrawn from one laboratory sample or from replicate laboratory samples (b) shall be used for the purpose of identifying the STMR or HR value or estimating the maximum residue level.

6.3.1 Treatment of apparent outliers

Residue values above the majority of the population have to be treated individually and should only be disregarded if there is adequate information, experimental evidence to justify their exclusion. At the time of evaluating the results, utmost care is required to decide that a result is invalid. The exclusion of an apparent outlier must be justified by agricultural practice or other evidence deriving from the experimental set up or analytical conditions.

6.3.2 Residues below LOQ

As a general rule, where all residue trials data are < LOQ, the STMR value would be assumed to be at the LOQ, unless there is scientific evidence that residues are "essentially zero". Such supporting evidence would include residues from related trials at shorter PHIs, exaggerated,

but related application rates or a greater number of applications, expectations from metabolism studies or data from related commodities.

Where there are two or more sets of trials with different LOQs, and no residues exceeding LOQ have been reported in the trials, the lowest LOQ should normally be used for the purpose of selection of the STMR value (unless the residues can be assumed to be essentially zero as given above). The size of the trials database supporting the lowest LOQ value should be taken into account in the decision.

The HR value should also be assigned a level of 0 when there is evidence that the residues are "essentially zero".

6.3.3 Rounding of residue values

In identifying the STMR or HR value from a residue trial, the actual residue value reported should be used in the estimation of dietary intake without rounding up or down. This would even be the case where the actual results were below the practical LOQ considered appropriate for enforcement purposes. Rounding of residue values is inappropriate since the STMR and HR value are used at an intermediate stage in the dietary intake calculation.

6.4 COMBINING OF DATA POPULATIONS

As a general precondition, for reliable estimation of residue levels an adequate number of independent trials are required which reflect the national maximum GAP and conducted according to well designed protocols that consider geographical distribution and the inclusion of a number of different growing and management practices, and growing seasons.

Under practical conditions the number of trials which can be performed for a given commodity is limited. On the other hand, a larger data set *representing statistically not different residue population* provides more accurate estimation of the selected percentile of residue population than a small data set derived from trials representing the critical 'one' GAP.

In estimating an STMR, the JMPR evaluates whether data sets for a given commodity or commodity group should be combined and whether residue data reflecting different countries' GAPs should be combined, provided that the GAP-s are similar.

The inevitable sampling variation may lead to an inaccurate estimation of the true residue population resulted from the use of a pesticide according to maximum GAP. In deciding whether the results of trials reflecting different countries' GAPs give rise to different populations of residues data, the size of the database reflecting the different countries' GAPs should be taken into account. Statistical tools are available that can be used to ascertain if data sets come from populations characterized by similar median/mean and variance.

In view of the skewed distribution of residues and the difficulties of describing the residue distribution with parametric methods, distribution free statistical methods should be applied for testing the similarity of sample populations.

Statistical tests are useful tools in the evaluation of pesticide residue trial data. However, due to the complexity of the task, which includes the consideration of several factors such as metabolism and rate of disappearance, such tests are not definitive and can only support expert judgement.

The field to field variation of residues skewed towards the high values do not follow normal distribution, even if this might be indicated by statistical tests based on small data sets.

Consequently, distribution free statistics should be used for comparing two or more residue data sets.

The JMPR routinely use the Mann-Whitney U-test in comparing two data sets to assess whether they can be combined. For cases where more than two data sets are to be compared the U-test is not applicable, in which case the Kruskal-Wallis H-test may be used. Their principles are explained in the next sections, and the calculation can be performed automatically with the Excel template which can be downloaded from http://udel.edu/~mcdonald/statkruskalwallis.html. As usual if the calculated probability is larger than 0.05 the null hypothesis is accepted and the data sets can be combined.

6.4.1 The Mann-Whitney U-test

Test statistics (U_1 and U_2) are calculated using the individual results from both residue populations and then the smaller test statistic is compared to a tabulated critical value (α_2=5%). Where the test statistic is less than or equal to the tabulated value, the two median values are considered to be similar.

The JMPR has agreed to combine residue populations where GAPs were similar and where the U-test suggested their medians are similar and to use the combined population for the estimation of maximum residue levels and STMR values. Where the populations are different, only the population which contained the highest valid residue value for both estimates is used.

Example: tebufenozide

Residue populations of mandarin and orange flesh from Italy and Spain were compared using the Mann-Whitney U-test to determine whether the populations were similar or different.

Residues in mandarin flesh: 0.069, 0.076, 0.082, 0.092, 0.14, 0.18 mg/kg

Residues in orange flesh: 0.021, 0.03, 0.04, 0.04, 0.05, 0.053, 0.11, 0.13, 0.13, 0.15 mg/kg

The test statistics, U_1 and U_2 values, are calculated as:

$$U_1 = n_1n_2 + [n_1(n_1+1)]/2 - \Sigma R_1$$

$$U_2 = n_1n_2 + [n_2(n_2+1)]/2 - \Sigma R_2$$

Where:

- n_1 and n_2 are the number of data points in populations 1 and 2 respectively (n_1 and ΣR_1 are assigned to the smaller when the sample sizes are different)
- ΣR is the sum of ranks of the corresponding values

The calculation for Mann-Whitney U-test is shown in Table 6.1

1. In a table, list all the measurements from lowest to highest. Use bold or coloured fonts to distinguish between the two data sets.

Table 6.1 Illustration of the calculations for the U-test

Residues (mg/kg)	Ranks for mandarins	Ranks for oranges
0.021		1
0.03		2
0.04		3.5
0.04		3.5
0.05		5
0.053		6
0.069	7	

Residues (mg/kg)	Ranks for mandarins	Ranks for oranges
0.076	8	
0.082	9	
0.092	10	
0.11		11
0.13		12.5
0.13		12.5
0.14	14	
0.15		15
0.18	16	
∑Rank	64	72
U values	$U_1 = 17$	$U_2 = 43$
Critical Value ($n_1 = 6$, $n_2 = 10$, $\alpha_2 = 5\%$)		11
$U_1 > 11$	Populations similar	

2. In a column for each population, place the corresponding ranks next to each measurement. For ties assign the average of the ranks, e.g., for 0.04, 0.04 the ranks are 3.5 and 3.5 instead of 3 and 4.
3. Calculate the sum of the ranks for each population.
4. Calculate the U values using the above equations ($U_1 = 17$; $U_2 = 43$).
5. Check the correctness of the calculation ($U_1 + U_2 = n_1n_2$).
6. Compare the lower U value with the tabulated critical value (Appendix XIII). The critical value is 11 ($n_1 = 6$, $n_2 = 10$). Since U_1 is greater than 11, it is concluded that the samples probably came from populations with the same median.

As the lower of U_1 and U_2 is greater than the critical value of 11 it can be concluded that the populations have similar distributions and can be combined for the purposes of estimating an STMR value. This conclusion has an effect on the calculation of the long-term intake of the residues, as the median values for the individual populations were 0.087 mg/kg for mandarin flesh and 0.0515 mg/kg for orange flesh instead of 0.079 mg/kg for the combined population.

6.4.2 Kruskal-Wallis H-test

Kruskal-Wallis H-test assumes that the samples are taken from continuous populations of similar shape, the errors in individual residue values are independent. It is applicable for ***k*** independent samples, provided that the data sets are not too small (≥ 4). For the purpose of the test, samples are independent if the supervised trials have been carried out at different sites.

The null hypothesis, H_0, is that the ***k*** independent sets of samples were taken from the same parent population. The alternative hypothesis is that the samples come from different populations. However, if the null hypothesis is rejected we do not know whether the median values, the shape or the variance of the tested populations are different.

The calculation is illustrated in Table 6.2 with the example of deltamethrin residues in leafy vegetables (2002 JMPR) and performed as follows:

The residue values belonging to the ***k*** data sets consisting of N_i residue values are marked with different colours and or letters to differentiate the data sets from each other.

Table 6.2 Illustration of the calculations for Kruskal-Wallis test for comparison of multiple independent samples

	Independent residue data sets			All residues	Corrected ranks	Corrected rank numbers for sample sets			Ties	T_j
	Curly kale	**Lettuce**	Spinach			Curly kale	Lettuce	Spinach		
No of data	8	10	16	34	34	8	10	16		
Sum of ranks, R_i					595	160	215.5	219.5	17	156
R_i^2/N_i						3200	4644.02	3011.27		
	0.07	**0.07**	0.03	0.03	1.5			1.5	2	6
	0.08	**0.12**	0.03	0.03	1.5			1.5		
	0.1	**0.13**	0.04	0.04	3			3		
	0.11	**0.15**	0.06	0.06	4			4		
	0.32	**0.18**	0.08	0.07	5.5	5.5			2	6
	0.32	**0.18**	0.09	**0.07**	5.5		5.5			
	0.34	**0.25**	0.09	0.08	7.5	7.5			2	6
	0.39	**0.26**	0.1	0.08	7.5			7.5		
		0.29	0.1	0.09	9.5			9.5	2	6
		0.41	0.1	0.09	9.5			9.5		
			0.1	0.1	13	13			5	120
			0.14	0.1	13			13		
			0.17	0.1	13			13		
			0.2	0.1	13			13		
			0.5	0.1	13			13		
			1	0.11	16	16				
				0.12	17		17			
				0.13	18		18			
				0.14	19			19		
				0.15	20		20			
				0.17	21			21		
				0.18	22.5		22.5		2	6
				0.18	22.5		22.5			
				0.2	24			24		
				0.25	25		25			
				0.26	26		26			
				0.29	27		27			
				0.32	28.5	28.5			2	6
				0.32	28.5	28.5				
				0.34	30	30				
				0.39	31	31				
				0.41	32		32			
				0.5	33			33		
				1.0	34			34		

Combine the residues from the ***k*** data sets in one data set consisting of $N=\sum N_i$ residue data, and arrange the residues in ascending order.

Determine the rank number of individual residues (r_i) giving the same rank for the same residue values (ties) and calculate the sum of the ranks (R_i) for each data set.

Calculate the H statistics and the correction factor (C_f) for the ties.

$$H = \frac{12}{N(N+1)} \sum_{i=1}^{k} \left(\frac{R_i^2}{N_i} \right) - 3(N+1)$$

The calculated H value is 4.465

$$C_f = 1 - \frac{\sum_j T_j}{N^3 - N}$$

Where $T_j = t^3 - t$, and t is the number of ties. For instance the residue values of 0.03 occur twice, so t =2 and $T_j = 2^3 - 2 = 6$. The value of 0.1 occurs 5 times, so t = 5 and $T_j = 5^3 - 5 = 120$.

Calculate the corrected H_c value:

$$H_C = \frac{H}{C_f}$$

The calculated Cf and Hc values are 0.9960 and 4.4829, respectively

The H_c value follows χ^2 (chi square) distribution with **ν = k-1** degrees of freedom. If $H_c \leq \chi 2_{0.05,\nu}$ the null hypothesis is retained, this indicates that the tested residue populations are not significantly different and can be combined for the estimation of maximum residue levels and STMR values.

The critical $\chi^2_{0.05}$ values are:

ν	2	3	4	5	6
$\chi^2_{0.05}$	5.9915	7.8147	9.4877	11.0705	12.5916

In our example ν = 3–1=2, the corresponding critical value is 5.99, consequently we can conclude that the three populations tested are not significantly different from each other and can be combined.

The performance of the Kruskal-Wallis test is facilitated by an Excel template, which performs the calculations for 7 data sets after inserting the residues composing of the data sets and arranging the ranks corrected for ties for each sample set.

The ranks are corrected for ties accurately if the sum of corrected ranks is equal to the total number of samples.

6.5 ESTIMATION OF MAXIMUM RESIDUE LEVELS

The JMPR examines the possibility of estimating maximum residue levels based on the residue values selected from submitted information and trial data, and subsequently proposes Maximum Residue Limits in commodities for pesticides used according to Good Agricultural Practice.

In estimating maximum residue levels, the FAO Panel takes into account all relevant information and especially the residues arising from supervised trials (see Chapter 3, Section 5 '*Residues resulting from supervised trials on crops*') and the congruence of the trial conditions and the established GAP. (See Chapter 3, Section 4 '*Use Patterns*' and Chapter 5, Section 6 '*Information on good agriculture practice*'.) The procedure for estimating and recommending Codex MRLs may be somewhat different from that applicable at national level as Codex MRLs cover residues derived from authorized uses worldwide and therefore reflect

a variety of agricultural practices and environmental conditions while at the national level MRLs are more related to the national GAP.

Although supervised residue trials are conducted according to the GAP prevailing at the time, GAP can often be modified by changes in the rate of application, the type of formulation, the method of application, the number of applications and PHI. Judgement is then required in order to determine whether the trial conditions are still close enough to GAP to be relevant.

6.5.1 Information considered in estimating maximum residue levels

The nominal rate of application in a trial would normally be considered still consistent with GAP when it is within approximately ±25% of the GAP rate, which includes the probable variation in commercial practice. When little or no residue is present, data from higher application rates may be important.

Formulations

*See sections **3**.5.1.2, **5**.3 and **6**.2*

Application method and number

The method of application can be quite influential on residue levels. For example, directed application is not comparable to cover spray, and aerial application may not be comparable to ground application.

For a non-persistent pesticide the number of applications is unlikely to influence residue levels. For a persistent pesticide the number of applications would be expected to influence residue levels. The nature of the crop should also be considered. For example, summer squash may be harvested only a few days after flowering; hence residues of a non-systemic pesticide applied before flowering would be expected to be low and the number of applications should have little influence on the residue level.

Pre-harvest interval

The pre-harvest interval usually, but not always, influences the level of residues found. (See section **6**.2."*Comparability of supervised trial conditions to GAP*").

Non-detectable residues

Some pesticide uses, such as seed treatments and pre-emergence herbicide treatments, usually lead to non-detectable residues in the final harvested commodity; but when many results are provided residues may be detected in occasional samples. While residues resulting from use according to GAP are most likely to be undetectable, the occasional detectable residues should not be ignored when a maximum residue level is estimated. Phorate on potatoes and residues arising from the pre-planting application of glyphosate are two examples.

Climate

Greater certainty that the climatic conditions are properly reflected in the supervised trials is afforded when the trials are carried out in a country with established GAP and reflect the range of climatic conditions and crop management practices within that country. Trials conducted in other countries with similar climatic conditions and crop management practices may be acceptable on a case-by-case basis. An assessment of those conditions is difficult, and a critical evaluation is needed as only some difference in conditions, such as temperature or intensity of sunlight, may be of great importance for the persistence of many pesticides and consequently for the residue level.

Crop description

The CCPR establishes MRLs on commodities as they move in trade to enable the control of compliance with and enforcement of GAP. Consequently, the maximum residue levels are estimated on a whole commodity basis (see Appendix VI) as far as practical.

The trials should be carried out with the same crops as those specified in the national GAPs. The proper description of the crops used in the supervised trials is important for deciding if crops referred to in GAP are in accordance with those for which trials have been carried out. Codex Classifications should be used for describing harvested commodities. A crop description such as "beans" is difficult to interpret because of the wide variety of beans grown. A more specific description is needed. Foliar application to head lettuce and leaf lettuce may produce different residue levels, so it may not be possible to use trials for a crop simply described as "lettuce".

Crop groups such as leafy vegetables, cole crops and grain legumes on national labels may not have the same meaning as the Codex commodity groups. It is necessary to check the crops included in a national label crop grouping.

Variability of residues

An awareness of the expected variability of residues is necessary. If the data truly reflect the range of conditions, application methods, seasons and cultural practices likely to be encountered commercially, then considerable variation in the resulting residue levels is expected. Analysis of supervised trials evaluated by the JMPR between 1997 and 2007 revealed that the coefficient of variation of residues between fields can sometimes be over 110%. Where copious data are available, consideration of the spread and variability of the residues helps to avoid misleading interpretations of small differences in estimates of the maximum level. Where only limited data are available, which is the case for the majority of supervised data sets (most frequently 8–9)[28] actual variability may be underestimated and judgement is required to arrive at an estimate that is realistic, practical and consistent. It is not a criticism to say that the data are widely spread and variable. If results have been obtained at a number of places over some years they are likely to be a better approximation to commercial practice and will be widely spread. In addition to the variability of residues within a confined area which can be considered uniform regarding climate, agricultural practices, pest situation and use recommendations, there may be an even greater variation of residues among areas of widely differing conditions, e.g., countries being in temperate, Mediterranean and tropical zones. The differences in use conditions can be so large that they result in different residue populations (see section **6**.4 "*Combining of data populations*").

Frequently the situation is complex even when much data and information is available. There can be alternative interpretations, and judgement is required to arrive at an estimate that is realistic, practical and consistent.

6.5.2 Principles of selection of residue data for estimation of MRLs

When estimating maximum residue levels, the FAO Panel examines all residue data arising from supervised trials supporting or reflecting the reported GAPs.

In the case of suspected multiple residue populations, limited data indicating the high population may not be sufficient to estimate a maximum residue level reflecting that population (and use pattern), and the FAO Panel may estimate a maximum residue level reflecting only those uses for which sufficient residue data are available. On the other hand, it

[28] FAO Pesticide Residues in Food 2008- Report. FAO Plant Production and Protection Paper No. 193 FAO, Rome.

is not possible to reconsider and reduce a previous estimate based on a new small trial data set indicating lower residues, unless the GAP on which the old recommendation was based has been changed or the original trials on which the MRL were estimated are now considered inadequate.

In accordance with the Codex definitions and general practice of the JMPR, the maximum residue levels are primarily estimated based on the GAP that leads to the highest residue (ONE GAP, the critical or maximum GAP), i.e., the trials represent the maximum residue anticipated when a pesticide is applied according to the one GAP (label directions, usually maximum permitted application rate, shortest PHI). Application should be made using equipment and spray volumes likely to give rise to the highest residues. The Codex Alimentarius definition (JMPR practice) implies that only the results of "supervised trials conducted at the highest nationally recommended, authorized or registered use" are included in MRL estimation, i.e., one maximum GAP per country, and one of these is used to select data for MRL estimation. To ensure the residue values selected for estimating maximum residue levels are independent, only one field trial would normally be selected per trial site if multiple plots/trials are conducted in parallel. See also section **6**.2.

The focus on the maximum GAP allows for alternative GAP to be assessed if there is an identified dietary intake problem. In such cases, where residue data permits, an alternative national GAP is considered and the supporting residue data sets are used for estimation of MRLs which do not raise acute intake concern.

Maximum residue level estimates may be based on an accepted/recognized extrapolation of trial data to cover commodities within a group which had shown a similar residue pattern. Principles used for the evaluation of data sets for one pesticide×commodity combination may be applied for evaluation of residues within one commodity group, e.g., application of 'one GAP' principle for estimating MRL for a group based on the highest residues data set obtained in one commodity.

There may be some situations which are not covered by the general principles outlined in this section. Such cases require a case-by-case consideration and expert judgement based on all available information and prior experience.

In cases, where only small number of residue data is available, MRL estimates should take into account:

- the highest values, median value and approximate 75th percentile value in the available data set of supervised residue trials
- residue levels resulting from application rates other than the label rate (for instance, using residues below LOQ in samples derived from double rate treatments to support no detectable residues following the application at maximum label rate, using highest residues from samples taken at longer intervals than PHI)
- experience of typical distributions of residue data from supervised trials
- knowledge of residue behaviour from the metabolism studies, e.g., is it a surface residue, does it translocate from foliage to seeds or roots
- knowledge of residue trials on comparable crops.

6.6 SPECIFIC CONSIDERATIONS IN ESTIMATING MAXIMUM RESIDUE LEVELS FOR INDIVIDUAL COMMODITIES

6.6.1 Fruits and vegetables

All the previously described general considerations apply for estimating maximum residue levels in fruits and vegetables. Applications on fruit and vegetables may take place at any stage of the developments of the plants and in the soil before and after sowing, and the residue levels are highly dependent on the treatment.

The pre-harvest interval (PHI) is usually an important component of GAP that has a strong influence on the resulting residues. It is especially important for fruit and vegetables for foliar application close to harvest. See Chapter 6 section 2 "*Comparability of supervised trial conditions to GAP*" for the latitude of acceptable intervals around the PHI.

The whole fruit residue level may sometimes be derived from residue data obtained separately for peel and pulp if the weights of peel and pulp are available.

6.6.2 Grains and seeds

Maximum Residue Limits for seeds or grains apply to the whole commodity. It is important for the JMPR to be able to distinguish between the forms in which the commodities are present and to describe the raw and processed commodities according to the Codex Commodity Classification, as some grains and seeds are still in the husks and others are without husk. Sometimes residues are reported in polished rice. The residue levels are usually considerably different for those sorts of commodities. The estimation of the maximum residue levels should be based on residues in commodities which may move in international trade.

When grains and seeds are milled, the commodities belong to the processed commodities.

6.6.3 Forage and fodder

Pesticides are needed in the production of animal forage and fodder crops, so residues in the resulting forage and fodder may be expected.

The succulent or high-moisture stages of the crop are known as forage and mostly are grazed directly or are cut and fed to livestock without delay. Examples are: maize forage, alfalfa forage and pea vines. The dry or low-moisture stages of the crop are known as hay, straw or fodder, which may be readily stored and transported as commodities of trade.

In the past, JMPR has recommended MRLs for forage crops and has used information on their residue status in estimating farm animal dietary burden. The 2002 JMPR decided that forage was not an item of international trade requiring Codex MRLs and would no longer recommend MRLs for forage commodities. Forage residue data would continue to be evaluated and used in the estimation of farm animal dietary burden.

MRLs are recommended for fodder which is an item in international trade.

6.6.4 Animal products

When residues occur in crops and animal feeds there is the potential for residues to be transferred to animals. The results of farm animal feeding studies and residues in animal feed and processing by-products of food serve as a primary source of information for estimating animal commodity maximum residue levels (See also Chapter 3 section 9 "*Information and data from farm animal feeding and external animal treatment studies*" and Chapter 6 section

12 "*Estimation of maximum residue levels and STMR values for commodities of animal origin*"). In addition, animal metabolism studies may also provide useful information.

Uptake of pesticides by animals can lead to residues in animal products following either direct application of the pesticide to the animal or its housing, or ingestion of feed containing pesticide residues.

Animal feeds with residues of pesticides may derive from:

- crops produced mainly for animal feed, e.g., pasture, straw, forage,
- crops produced mainly for human food which are fed to animals, e.g., cereal grains,
- waste from crops grown primarily for human food, e.g., skins, pulp, stems, stubble or trash,
- animal feeds that have not themselves been treated, but in which environmental contaminants occur, for example, from crops or pastures grown in DDT contaminated soil.

When animals are fed, the potential for dilution of feed residues is considerable. Not all producers of the primary crop are likely to have used the same pesticide simultaneously, and the pesticides used are not always used at their highest permitted use rates or at the nearest time to harvest. However, the animals could be exposed for extended periods to certain commodities such as fodder, grain and feeds treated post-harvest which contain residues at the highest level[29]. For example, on a farm on which 20 ha of an animal feed (forage, fodder or grain) were grown per year with a yield of 10 t/ha on a dry weight basis, enough would be produced to feed 333 head of cattle for 1 month. If the feed constituted less than 100% of the diet, more head of cattle could be fed for 1 month, or the duration of feeding might be longer. On the other hand, it is unlikely that the individual ingredients of mixed feeds produced from commercially available ingredients would all contain residues at the theoretical maximum level. Consequently, the highest residues in individual feed items are used for estimating the maximum residue levels in animal commodities, and the STMR or STMR_P should be applied to each of the components of mixed commodities.

The 2002 JMPR[30] recognized that the practice followed in species selection for the recommendation of maximum residue levels for animal tissues, milk and eggs has not always been consistent. Following an evaluation of the results of animal transfer studies and taking into account current practices in many countries, the Meeting decided that when residues in animal products arise from residues in feeds, in general, the results of cattle feeding studies may be extrapolated to other domestic animals (ruminants, horses, pigs, rabbits and others) and laying hen feeding studies to other types of poultry (turkey, goose, duck and others). The suite of maximum residue levels recommended should be selected from: MM 0095 Meat (from mammals other than marine mammals)[31], MO 0098 Kidney of cattle, goats, pigs and sheep, MO 0099 Liver of cattle, goats, pigs and sheep and ML 0106 Milks. Where residues in liver and kidney are essentially the same or nil, an option is to recommend a MRL for MO 0105 Edible offal (Mammalian). Maximum residue levels should be recommended for

[29] FAO,Pesticide residues in food, Report 2004, FAO Plant Production and Protection Paper No. 178 FAO, Rome p. 26

[30] FAO, Pesticide residues in food, Report 2002, FAO Plant Production and Protection Paper No. 172 FAO, Rome p. 22

[31] muscular tissues with trimmable fat removed. For fat-soluble pesticides a portion of adhering fat is analysed and MRLs apply to the fat.

poultry and selected from: PM 0110 Poultry meat[32], PO 0111 Poultry, Edible offal of[33] and PE 0112 Eggs.

The 2002 JMPR also noted that extrapolation based on direct animal treatment is generally not justified as there are significant species differences in residue transport through skin and in animal behaviour, e.g., grooming in cattle but not in sheep, that have implications for possible residues in tissues. Therefore, when residues arise from direct application to animals the resulting MRLs should relate to the species stated on the registered label and the animal studies provided, i.e., if the label use specifically applies to sheep MRLs should only apply to sheep commodities (meat, offal). The JMPR agreed that extrapolation to a second species would be considered where the uses were similar and where past experience suggests sufficient comparability between species.

The information from the animal metabolism and feeding studies and the likely levels of residues should support the decision to extrapolate. Extrapolation is encouraged to the group when there is no reason to expect higher residues than in cattle.

Some compounds are very readily metabolised or are quickly broken down in the presence of animal tissues, eggs or milk. In such cases the parent compound and sometimes their primary metabolites are not found in animal tissues, eggs or milk following exposure of animals to residues in their feed, irrespective of the feeding levels. Consequently, monitoring programs are unlikely to detect residues of such compounds in animal commodities.

When suitable farm animal metabolism and feeding studies and analytical methods are available for such compounds JMPR recommends MRLs at or about the LOQ for animal commodities. These recommended MRLs indicate that the situation has been fully evaluated and that, for the commodities moving in trade, residues should not occur above the stated LOQ. In such cases, a footnote is inserted under the recommended MRLs stating that '*no residues are expected from consumption of feed commodities with [xxx pesticide] residues as evaluated by JMPR'*.

Meat

For pesticides which are not fat-soluble, maximum residue levels are estimated for muscle tissue and recommended for use as MRLs for meat.

For fat-soluble pesticides, maximum residue levels are estimated based on residues in trimmable fat expressed on the lipid content. For those commodities, e.g., rabbit meat, where the adhering fat is insufficient to provide a suitable sample, the whole meat commodity (without bone) is analysed and the maximum residue level is estimated on the whole commodity basis.

Edible offal

The maximum residue levels are estimated on a whole commodity basis.

Milk and milk products

For milk it is known that the fat content varies widely among different breeds of dairy cattle. In addition, as there are a large number of milk products, with varying fat content, it would be impractical to propose separate MRLs for each product. It was therefore originally decided to

[32] muscular tissues including adhering fat and skin from poultry carcasses as prepared for wholesale or retail distribution. For fat-soluble pesticides a portion of adhering fat is analysed and MRLs apply to the poultry fat.

[33] such edible tissues and organs, other than poultry meat and poultry fat, from slaughtered poultry as have been passed fit for human consumption. Examples: liver, gizzard, heart, skin.

estimate MRLs for fat-soluble compounds for milk and milk products on a fat basis, i.e., the residue levels expressed as if wholly contained in the extracted fat.

The JMPR had followed the CCPR convention[34], until 2007, of expressing the MRL for fat-soluble compounds in milk on a calculated whole product basis, assuming all milks contained 4% fat. (The residue is calculated for the whole product based on the residue measured in the fat.) For compounds which are not fat-soluble, the analytical portion for enforcement purposes is whole milk and MRLs are expressed on a whole milk basis. Many pesticides, however, have intermediate solubility in fat; even if they are regarded as fat-soluble, they can be distributed equally between the fat and non-fat portions of milk.

The 2007 JMPR decided that, for fat-soluble pesticides, two maximum residue levels would be estimated, if the data permitted. One MRL for whole milk and one for milk fat. For enforcement purposes, a comparison can be made between either the residues in milk fat with the MRL for milk (fat), or the residue in whole milk with the MRL for milk. When needed, maximum residue levels for milk products can then be calculated from the two values, by taking into account the fat content of the milk product and the contribution from the non-fat fraction. The 2008 CCPR agreed[35] that for regulation and monitoring of residues of fat-soluble pesticides in milk, where MRLs have been established for both whole milk and milk fat, whole milk should be analysed and the result should be compared with the Codex MRL for whole milk. The Committee asked the JMPR to insert a footnote to this effect for MRLs for whole milk in all cases where the MRLs have been established for both milk fat and whole milk.

Details of expressing residues in milk and milk products are given in this chapter in section 13 "*Expression of maximum residue limits.*"

Eggs

For eggs, the maximum residue level is estimated on the whole commodity after removal of the shell.

6.7 ESTIMATION OF GROUP MAXIMUM RESIDUE LEVELS STMR AND HR VALUES FOR PLANT COMMODITIES

The establishment of commodity group MRLs as opposed to MRLs for individual commodities has long been considered an acceptable procedure at both the national and international levels. The use of the approach recognises that economics may not justify residue trials on all of the individual crops in a group. It also follows logically national registration systems where the registered use may be on a crop group, such as citrus. In principle the approach recognizes that adequate data for the major crops of a group may be sufficient to estimate maximum residue levels for the whole group.

Some pesticides may behave differently in different circumstances. Consequently, it is not possible to define precisely those commodities on which trials will always provide data that can lead to a group MRL. If the "highest residue" situation can be identified, however, the relevant data can be extrapolated to other crops with confidence, although it is recognised that this approach may result in an over-estimate of residues in some commodities. An acceptable

[34] FAO/WHO 2000: Codex Alimentarius Volume 2B, Pesticide Residues in Food – Maximum residue limits. Joint FAO/WHO Food Standards Programme, page 4. Rome, 2000.

[35] Report of the fortieth session of the Codex committee on pesticide residues *2008,* Alinorm 08/31/24, para 125 and 161, http://www.codexalimentarius.net/web/standard_list.do?lang=en

example is extrapolation of residue data from gherkins to cucumber; however, the converse is not possible due to the higher residues that can be expected in gherkins as a consequence of the difference in surface/weight ratio.

Extrapolation requires a detailed knowledge of local agricultural practices and growth patterns. For example, wheat is generally grown under similar practices around the world, but grapes may be grown utilising widely varying practices. For the latter, care must be taken to ascertain if the relevant GAPs are comparable. In view of the large differences in commodity surface texture, shape, plant growth habits, rate of growth and seasonal cultivation and the significant role played by the surface/weight ratio, the JMPR has emphasized that decisions to extrapolate should be made on a case-by-case basis when adequate relevant information is available.

As many factors can influence a decision to propose a group MRL the JMPR approaches the issue of setting group or individual MRLs on a case-by-case basis. The potential complexity of the process is highlighted by the current lack of international consensus on suitable criteria. These considerations have prevented the JMPR from developing specific guidance for group MRL estimation that might be applied at the international level.

Although no specific guidance is available, the following general principles and observations reflect the current views of the JMPR on estimating group MRLs.

a. The use pattern (rate, application method, timing, PHI) should be the same and applicable for the whole crop group. Crops within a crop group should have similar physical nature, growth pattern and production characteristics, similar cultural practices and similar pests that require the same pesticide treatment.

b. The nature of residues: systemic or non-systemic, degradation/disappearance rate.

c. Relevant and adequate residue data should be available for at least one major commodity of the group. (However, all relevant data for the commodities of the group should be taken into account including Residue levels measured across several crop or commodity types.)

d. The JMPR continues to rely on the Codex Classification of Foods and Feeds as the primary basis for recommending MRLs for individual or grouped commodities. The distinction between the crop group and the commodity group should be noted. The distinction is not always clear because the same words are used to describe the crop and the commodity, e.g., in one context, "pineapples" can mean the crop in the field and in another context "pineapples" can mean the fruit itself. For field uses, pesticides are applied to the crop, so it is the crop or crop group that should appear on pesticide product labels. MRLs and residues are expressed on commodities, so commodities and commodity groups appear in MRL tables.

e. Generally the JMPR now refrains from estimating maximum residue levels for large Codex ‘classes’ of foods or feeds such as fruits, vegetables, grasses, nuts and seeds, herbs and spices, or mammalian products. Residue data and approved uses are usually more likely to refer to smaller Codex ‘groups’ such as pome fruits, citrus fruits, root and tuber vegetables, pulses, cereal grains, cucurbit fruiting vegetables, milks, meat of cattle, pigs and sheep. As well as being more likely to be supported by the available residue data and information on GAP, this approach is considered to be more in line with current national approaches and affords a more accurate estimation of dietary intake.

f. In some cases the JMPR may, in the absence of sufficient data for one commodity, use data from a similar crop for which GAP is similar to support estimates of maximum residue levels, e.g., pears and apples or broccoli and cauliflower.

g. After dietary intake assessment, commodity group MRLs may be proposed on the following minimum conditions[36]:

   - The pesticide is registered or authorized for use on the crop group;
   - Relevant and adequate residue data are available for at least one major commodity of the group. (However, all relevant data for the commodities of the group should be taken into account.) If the recommended group MRL is subsequently found to be inadequate for some commodities and their registered uses, there would be no impediment to submission of further data to amend the group MRL or to propose specific commodity MRLs.
   - In line with the alternative GAP proposal, if the IESTI calculations suggested that short-term intake would exceed the ARfD of the compound for one or more commodities in the group, the JMPR would examine and recommend alternative proposals including alternative GAP and single commodity MRLs.

h. If other considerations permit, data on residues in one or more of the major commodities with the potential for high residues within a group may allow estimates of maximum residue levels to be extrapolated to minor crops in the group. An example of where other considerations do not permit such extrapolation is where the variability of the residue levels is too great, despite there being data available on the major crop within the group. In such circumstance a group limit cannot then be estimated.

i. When residue levels in a number of commodities in a group vary widely, separate recommendations should be made for each commodity. A limit for a group 'except one or more commodities' which are known to deviate from the norm may be justified, e.g., citrus fruits, except mandarins; in such cases separate MRLs should be estimated for the exceptional commodities.

j. Residue data for a crop growing quickly in summer cannot be extrapolated to the same or related crops growing slowly under less favourable conditions, e.g., from summer to winter squash.

k. In establishing group MRLs, detailed knowledge of the metabolism or mechanism of disappearance of a pesticide in one or more crops must be taken into account.

l. Group MRLs recommended by the JMPR that generally appear to be acceptable include those listed in Table 6.1

m. All else being equal, data may sometimes be extrapolated from a crop picked when immature but which grows quickly to maturity, to a closely related species with a lower surface area/weight ratio. Thus, because of dilution by crop growth, estimated maximum residue levels can be extrapolated from gherkins to cucumbers, but not vice versa.

[36] Report of the 39th Session of the CCPR (2007) para 34

n. Individual MRLs can be extrapolated more readily to groups when there is no expectation that terminal residues will occur and when this is supported by studies of metabolism. Examples are early treatments, seed treatments and herbicide treatments in orchard crops.

While the JMPR generally follows these principles on a case-by-case basis, it recognizes certain difficulties or limitations in the acceptance of group limits at the international level. A primary weakness is the lack of formal criteria or an agreed mechanism to determine the members of a group for which data are needed before a group MRL can be established. One approach, as occasionally used at the national level, is to identify commodities of a group (often botanical) that represent both major crops within the group and those most likely to contain the highest residues. The factors used to determine whether a crop is a major or representative member of the group include its dietary significance as a food or feed.

Table 6.1 Examples for commodity groups and mutual support for estimation of maximum residue levels

Compound	Commodities with data supporting MRL	Group or commodities with MRL recommendation	Code
Pirimicarb	mandarin, orange	citrus fruits	FC
Thiabendazole	mandarin, orange	citrus fruits	FC
Bifenazate	apple, pear	pome fruits	FP
Fludioxonil	apple, pear	pome fruits	FP
Pirimicarb	apple	pome fruits	FP
Thiacloprid	apple, pear	pome fruits	FP
Bifenazate	apricot, cherry, peach	stone fruits	FS
Pirimicarb	cherry, nectarine, peach, plum	stone fruits	FS
Pyraclostrobin	cherry, peach, plum	stone fruits	FS
Thiacloprid	peach, sweet cherry	stone fruits	FS
Pirimicarb	currant, gooseberry, raspberry	berries and other small fruits (except grapes and strawberries)	FB
Thiacloprid	currant, raspberry, strawberry	berries and other small fruits (except grapes)	FB
Endosulfan	avocado, custard apple, mango, papaya	mutual support: avocado, custard apple, mango, papaya	FI
Endosulfan	litchi, persimmon	mutual support: litchi, persimmon	FI
Pirimicarb	broccoli, Brussels sprouts, cauliflower, cabbage	Brassica vegetables	VB
Bifenazate	cantaloupe, cucumber, summer squash	cucurbit fruiting vegetables	VC
Propamocarb	cucumber, melon, summer squash	cucurbit fruiting vegetables	VC
Pirimicarb	cucumber, summer squash	cucurbit fruiting vegetables (except melons and watermelons	VC
Thiacloprid	melon, watermelon	mutual support: melon, watermelon	VC
Pirimicarb	sweet peppers, tomato	fruiting vegetables other than cucurbits (except mushrooms, fungi, sweet corn)	VO
Pirimicarb	beans, peas	legume vegetables (except soybeans)	VP
Propargite	dry beans, dry broad-bean, dry chick-pea, dry lupin	mutual support: dry beans, dry broad-bean, dry chick-pea, dry lupin	VD
Pirimicarb	dry beans, dry peas	pulses (except soybeans)	VD
Endosulfan	potato, sweet potato	mutual support: potato, sweet potato	VR
Pirimicarb	carrot, potato, sugar beet	root and tuber vegetables	VR
Endosulfan	hazel nuts, Macadamia nuts	mutual support: hazel nuts, Macadamia nuts	TN
Bifenazate	almond, pecan	tree nuts	TN
Thiacloprid	almond, pecan, walnut	tree nuts	TN
Aminopyralid	barley, oats, wheat	barley, oats, wheat, triticale	GC

Compound	Commodities with data supporting MRL	Group or commodities with MRL recommendation	Code
Pirimicarb	barley, maize, wheat	cereal grains (except rice)	GC
Pirimicarb	barley straw, maize fodder, wheat straw	straw and fodder of cereal grains except rice	AS
Aminopyralid	barley straw, oats straw, wheat straw	straw of barley, oats, wheat and triticale	AS

The premise of this approach is that if data are available for representative crops, and if GAP and cultural practices among the individual members are similar, the residue levels should not vary widely then a maximum residue level can be estimated that will suffice for those members of the group for which no data are available. This approach is necessitated by the economics of data generation and evaluation requires the use of common sense and expert judgment.

While the JMPR acknowledges advantages in this approach, there is unfortunately no consensus at the international level on the selection of representative commodities for estimating maximum residue levels for groups. Similarly, while the JMPR bases its recommendations on the Codex Classification of Foods and Feeds, this classification has not been uniformly adopted at the national level.

Until agreement is reached at the international level, the JMPR will continue to make judgements on a case-by-case basis, using the general policy summarized above or as it may be subsequently amended.

6.7.1 Estimation of HR and STMR values

Where there are adequate trials data the STMR values should, in principle, be identified for the individual commodities and these values used for the intake assessment. However, where the MRL has been recommended for a group of commodities, e.g., pome fruit, a single STMR value should be calculated for the group of commodities.

Large portion size and unit weights are available for single commodities, not for commodity groups. Consequently, when an HR value is identified for a commodity group it can be used only on single commodities for IESTI calculation. The IESTI calculations for a group HR should be applied to the key commodities of the group for which large portion size and unit weight data are available, especially to those commodities with data supporting a MRL estimation.

6.8 EXTRAPOLATION OF RESIDUE DATA TO MINOR CROPS

Section 6.7 outlined the process involved in the estimation of group maximum residue levels, provided examples and discussed limitations. Data considered adequate for the estimation of an MRL of a major crop, of a group, are considered generally sufficient to estimate maximum residue levels for the whole group, including the minor crops of that group.

However, decisions to extrapolate from one or more major crops to minor crops are taken by JMPR are on a case-by-case basis when adequate information is available. Adequate information includes information on GAP for the relevant crops, a reference to the residue data used to support the original MRL, and an explanation of the logic for the extrapolation.

The data submitted to support extrapolation to a minor crop must include the following information.

- Background information on the reasons for describing the crop as minor, the importance of the use of the pesticide in terms of pests controlled, the extent of its use on the minor crop, and the nature of the problems or potential problems for international trade
- A description of the cultural practices for the production of the major crop and the approved or registered uses of the pesticide on the major crop from which extrapolation is proposed
- A description of the cultural practices for the production of the minor crop, the approved or registered uses of the pesticide on the minor crop, and the reasons for expecting similar residue levels on the minor crop to those of the major crop
- Supervised residue trials on the major crop supporting the MRL or reference to the JMPR Evaluations, if trials data have previously been reviewed by the JMPR.

The data submission should also include the following supporting information where available.

- Data on supervised trials with approved or registered uses on the minor crop
- A copy of the label describing the registered or approved uses and an English translation of the instructions for use
- Monitoring data from selective surveys on the minor crop produced under typical commercial conditions where the pesticide is known to have been used.

6.9 PROCESSED COMMODITIES

6.9.1 General principles

The use of data on the effects of processing or cooking practices on residue levels in RAC for estimation of processing factors is described in Chapter 5**.**Section 8 "*Processing studies*"

The best estimate of the processing factor should be applied for the estimation of maximum residue level, HR-P and STMR-P in processed commodities.

To estimate a maximum residue level for a processed product the MRL or maximum residue level of the RAC is multiplied by the processing factor. For the purpose of IEDI estimation, the STMR of the RAC is multiplied by the processing factor to give the median residue in the processed commodity. The HR, STMR value estimated in this way for the processed commodity should be referred to as the HR-P and STMR-P of the processed product.

Maximum residue level for the processed commodity will only be recommended if the resulting residue value is higher than the maximum residue level proposed for the corresponding RAC.

HR-Ps and/or STMR-Ps for commodities for human consumption are estimated regardless of the availability of consumption data.

If data are available for the residues in the edible portion of the commodity, e.g., in banana pulp, the HR and STMR should be estimated directly from the residues in the edible portion found in supervised trials at the maximum registered use rate (as opposed to using pesticide residue values for the whole commodity).

If these data are not available for the edible portion, the whole commodity residue values are used in the dietary intake estimations, even though this may result in a gross over-estimate of the actual residues likely to be consumed.

6.9.2 Special considerations for dried chili peppers

As a special case the CCPR agreed for dried chili peppers, a very minor crop, that a generic factor can be used for conversion of residues from fresh peppers to dried chili peppers. The JMPR evaluated the available information and used the concentration factor of:

- 10 for the estimation of residue levels of pesticides in dried chili peppers from the HR values estimated for residues in or on sweet peppers;
- 7 for the estimation of residue levels in dried chili peppers from maximum residue levels in or on fresh chili peppers.

The 2007 JMPR recommended that:

- where representative processing studies on residues in or on chili peppers are available, the residue levels for dried chili peppers should be estimated based on the actual experimental data
- the relevant concentration factor should be applied to multiply the actual measured residue values in fresh chili peppers, and estimate the maximum residue and median residue levels from the converted data set.

6.10 STATISTICAL METHODS FOR ESTIMATION OF MRLS FOR PLANT COMMODITIES BASED ON SUPERVISED TRIAL DATA

Some regulatory agencies use statistically based calculation methods to facilitate harmonised estimation of maximum residue levels, i.e., aimed at obtaining the same MRL estimates by different evaluators from the same residue data set. It has also been suggested that application of appropriate, validated statistical methods would also improve the transparency of Codex maximum residue level estimation and, consequently, might lead to their wider acceptance at the international level.

The FAO Panel currently applies statistical methods to assist in the selection of similar data populations, and, where the data package is suitable, takes into account statistical considerations, e.g., evaluations of aldicarb residues in potato (1996), EMRL recommendations for DDT residues in meat (2000), and estimation of MRLs for spices (2004).

The FAO Panel has therefore welcomed the development and availability of the NAFTA statistical calculation method, described in the NAFTA paper Statistical Basis of the NAFTA Method for Calculating Pesticide maximum Residue Limits from Field Trial Data[37]. The NAFTA spreadsheet[38] is a decision-tree logic (Figure 6.2 Chapter 6, Section 10) that utilizes statistical calculations to arrive at maximum residue level that should be acceptable to different parties considering the same data set. The spreadsheet looks only at numbers and not at the basis of those numbers. It is designed to give a consistent decision, independent of the prejudice of the reviewer(s). Detailed instruction for its use can be downloaded from

[37] Statistical Basis of the NAFTA Method for Calculating Pesticide maximum Residue Limits from Field Trial Data US EPA and Canada PMRA, May, 2007: EPA-HQ-OPP-2007-0632-0002

http://www.regulations.gov/fdmspublic/component/main?main=DocketDetail&d=EPA-HQ-OPP-2007-0632

[38] http://www.pmra-arla.gc.ca/english/pdf/mrl/method_calc_v2.xls

http://www.pmra-arla.gc.ca/english/pdf/pro/pro2005-04-e.pdf. Where more than 10% of the residue data are below the LOQ, the maximum likelihood estimation (MLE) spreadsheet, assuming lognormal distribution of residue data, should be used to convert the < LOQ values to real numbers. Based on the MLE parameters, fill-in values consistent with the associated lognormal distribution are calculated for the censored data points. These fill-in values are generally considered more appropriate than standard imputed values such as ½ LOQ when calculating summary statistics and statistical intervals for lognormal distributions, such as those calculated using the NAFTA tolerance spreadsheet. The effect of the converting the residue data to the postulated lognormal distribution is illustrated in Figure 6.3 (Chapter 6, Section 10). It should be noted that the MLE assumes that the data set follows a lognormal distribution which is the case in about 70% of residue data sets. If the residue data does not follow lognormal distribution, the use of MLE methods will produce a biased estimate.

The spreadsheets for the calculations can be downloaded from the NAFTA website or can also be obtained from the joint FAO Secretary of the JMPR.

The output of the calculations is shown in Table 6.2 (Chapter **6**, Section 10). The spreadsheet automatically selects the best estimate for the MRL and indicates it with highlighted cell.

The NAFTA spreadsheet suggests the use of the 95/99 Rule where the residue data set contains more than 15 data points. The White Paper[39] states that MRL spreadsheet provides reasonable estimates with a relatively small range of calculated MRLs for sample sizes as small as 10. If the data set has less than 10 data points, the MRL calculations from the NAFTA spreadsheet have large probability of underestimating the true 95th percentile value and are not very precise.

The outcome of NAFTA simulations, using lognormal data populations, indicate that the failure rate is practically independent from the spread of residue data (CV) within the parent population, which enables the drawing of general conclusions from the simulated data. However, where the NAFTA procedure would be used alone for estimation of maximum residue levels based on 6 to 10 data points, which occurs frequently in the deliberations of the JMPR (Figure 6.4), the recommended MRL would be underestimated, i.e., it would be below the targeted 95th percentile of the residue data populations, in 27% and 20% of cases.

The FAO Panel have utilised the NAFTA procedure on various data sets in the estimation of MRLs since 2005, and concluded that the statistical spreadsheet can be used as a tool to assist evaluators in the estimation of maximum residue levels, but that the output could not be automatically applied. It is emphasised that expert judgement in the proper selection of residue data set is the key component in obtaining a reliable estimate for a MRL.

The 2008 JMPR concluded that statistical calculations, as part of the maximum residue level estimation process, should only be used where the data are suitable to yield valid conclusions. Considerations should include:

- data from a single population or the equivalent of a single population
- the data should be from a random sample or stratified random sample from the population
- sufficient data (≥ 15) should be available to minimize the errors of extrapolation to the required high percentile values

[39] Statistical Basis of the NAFTA Method for Calculating Pesticide Maximum Residue Limits from Field Trial Data http://www.regulations.gov/search/Regs/home.html#documentDetail?R=090000648026e8d0

- the number of residue values below the LOQ and the residue distribution around LOQ
- no statistical test should be applied for excluding potential outliers; residue data should only be excluded if experimental evidence indicates that the data is invalid.

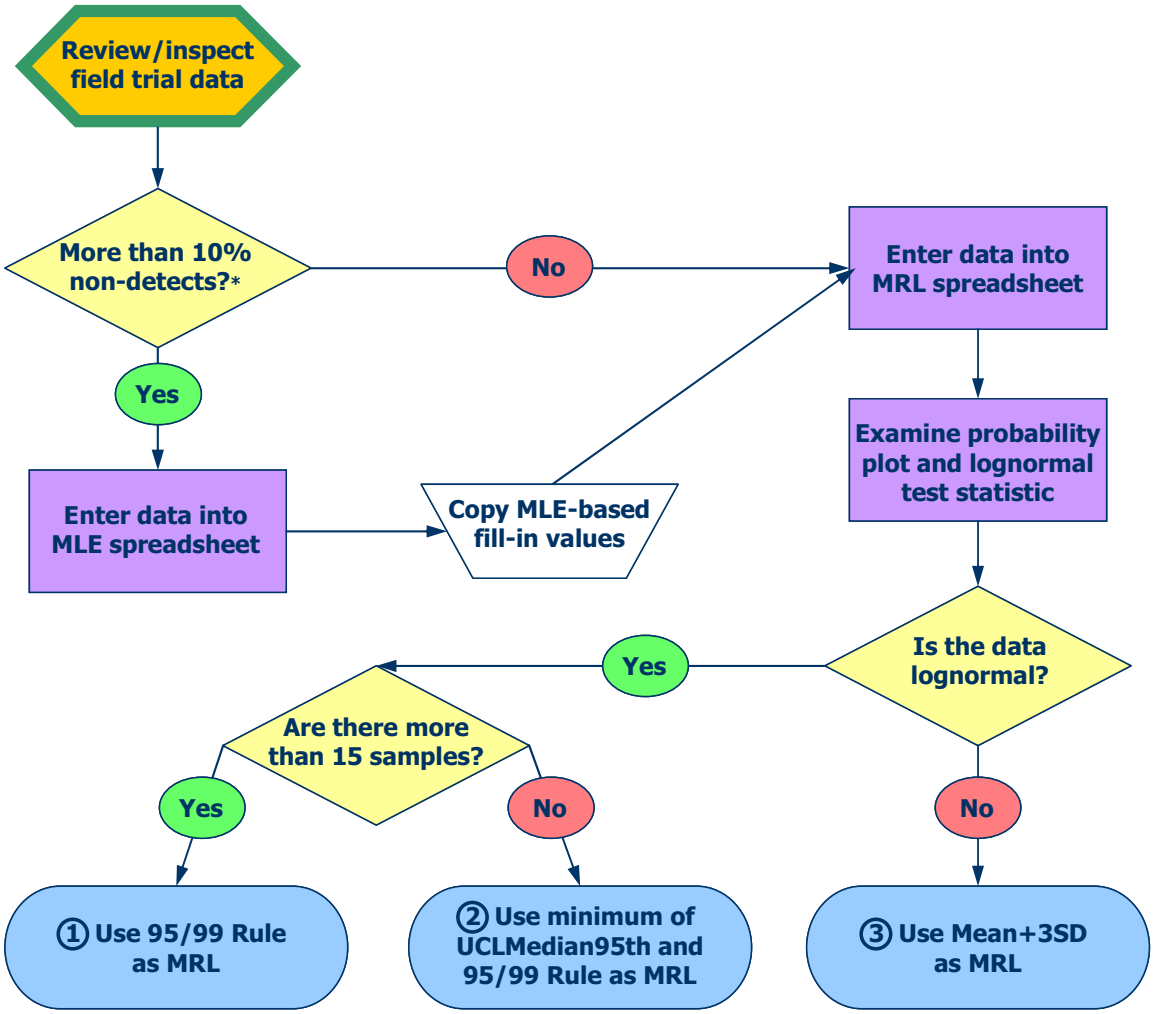

Figure 6.2 Decision tree for applying the NAFTA spreadsheet for obtaining the estimated maximum residue value

In cases, where only small number of residue data is available, MRL estimates should take into account:

- the highest values, median value and approximate 75th percentile value in the available data set of supervised residue trials
- residue levels resulting from application rates other than GAP (for instance, using residues below LOQ in samples derived from double rate treatments to support no detectable residues following the application at maximum application rate, using highest residues from samples taken at longer intervals than PHI)
- experience of typical distributions of residue data from supervised trials

- knowledge of residue behaviour from the metabolism studies, e.g., is it a surface residue, does it translocate from foliage to seeds or roots
- knowledge of residue trials on comparable crops.

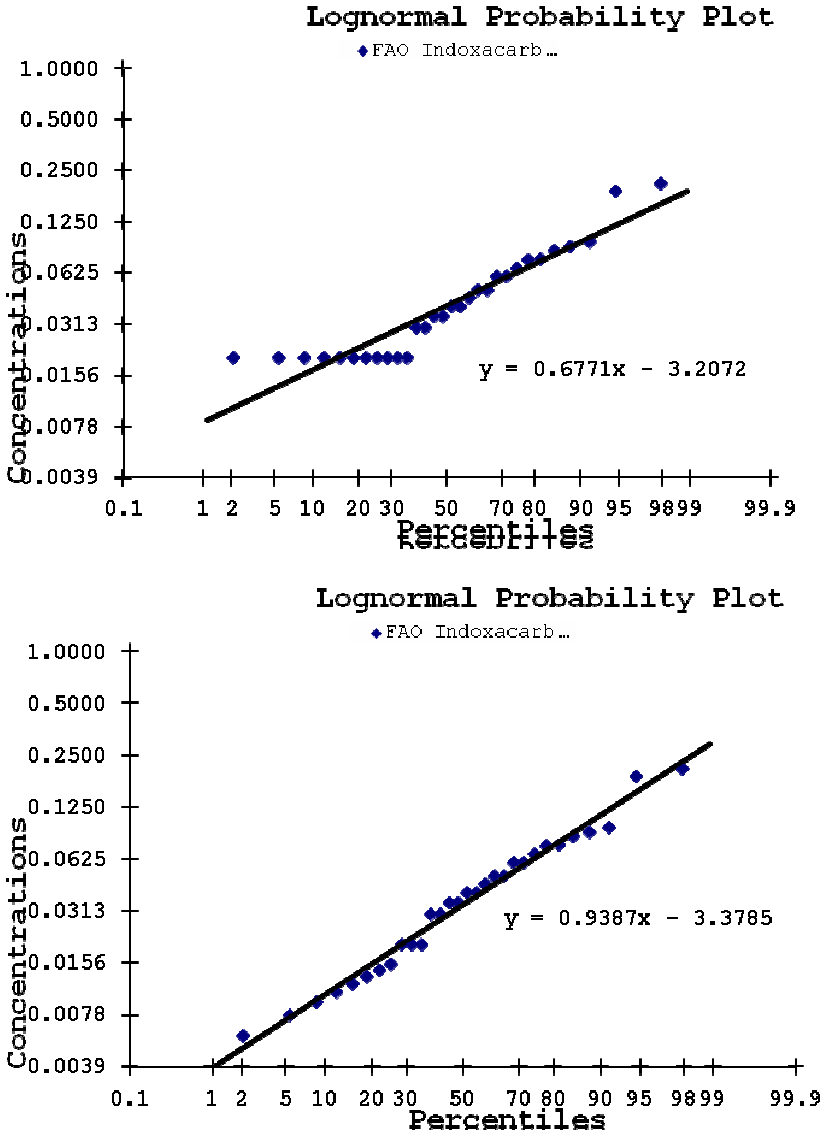

Figure 6.3 The lognormal probability plots based on original data (upper chart) and after fitting the residues reported as < LOQ to the most likely lognormal distribution (lower chart)

The use of the statistical spreadsheets provides information on the 95th and 99th/99.5th percentile of residue distributions. It was previously judged necessary to "round up" considerably on the value selected for the maximum residue level. This is no longer the situation where the statistical estimation tools are utilized. In order to more fully reflect the impact of this new tool, the Meeting concluded that the scaling steps last presented in the 2001 JMPR Report would replaced by a refined scale (see Section **6.**13 "*Expression of Maximum residue limits*")

Table 6.2 Output of NAFTA calculation

	Regulator: EPA Chemical: Pymetrozine Crop: Leaf Lettuce PHI: 0-1 Day App. Rate: Submitter:		
	n: 14 min: 0.14 max: 1.94 median: 0.77 average: 0.83		
	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	1.7 (2.5)[b]	2.0 (3.0)	2.5 (–)
95/99 Rule	2.5 (4.5)[d]	3.5[c] (9.0)	6.0 (–)
EU Method II Distribution-Free	2.5[e]		
Mean+3SD	2.5[f]		
UCLMedian95th	5.0[g]		
Approximate Shapiro-Francia Normality Test Statistic	0.9503p-value > 0.05 : Do not reject lognormality assumption		

[a] Tabled values in parentheses indicate 95% upper confidence bounds on the point estimates of the 95th or 99th percentiles. No upper confidence bounds on the 99.9th percentile are provided and these are represented by "(--)". Tabled values that are shown directly without parentheses represent point estimates of the indicated percentile (e.g., 95, 99, or 99.9)

[b] This is the MRL estimate that would be produced by EU Method I. It is the 95% upper confidence limit on the 95th percentile, but assumes that the residues are distributed normally.

[c] This is the estimated 99th percentile value assuming a lognormal distribution with the given mean and standard deviation.

[d] Lognormal distribution with the given mean, standard deviation, and sample size. If the residues are distributed lognormally, one can be 95% confident that 95% of the values in the parent distribution lie below this estimate.

[e] EU Method II. This method makes no assumption regarding the form of the distribution (e.g. normal, lognormal, etc.). It is calculated by doubling the 75th percentile of the residue values.

[f] This estimate is produced by adding 3 standard deviations to the mean. By Chebychev's Rule, at least 8/9 or 89% of measurements will fall within 3 standard deviations of the mean. This is true regardless of the shape of the frequency distribution.

[g] This value is calculated by estimating the 95th percentile from the upper confidence limit of the median value (50th percentile). It assumes a coefficient of variation of 1 and a lognormal distribution. In a lognormal distribution, the 95th percentile is 3.9 times the median. The value represented in this cell is 3.9 times the upper confidence limit on the median.

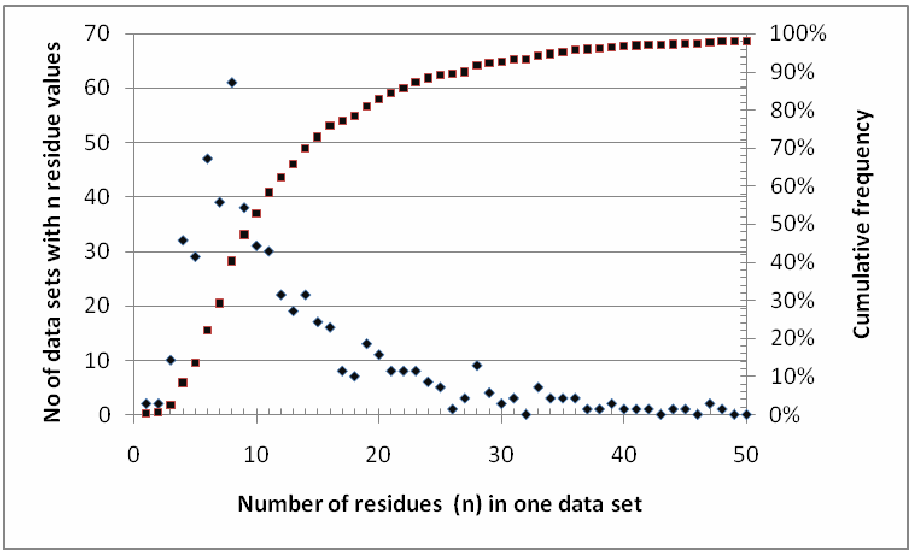

Figure 6.4: Frequency of occurrence of data sets consisting of *n* residue values used by JMPR between 2002 and 2007

The JMPR is aware of the need for harmonised approach in estimation of MRLs which would also facilitate work sharing, and looks forward to the further developments in statistical methods for estimation of MRLs such as being developed by the OECD Working Group on Pesticide Residues. The FAO Panel will apply the most reliable method available in combination with the general principles described in this and the previous sections.

6.11 ESTIMATION OF MAXIMUM RESIDUE LEVELS BASED ON MONITORING DATA

6.11.1 Estimation of maximum residue levels, HR and STMR values in spices

The 2004 CCPR accepted the definition of spices irrespective of whether they were classified as spices in the Codex Classification, and agreed to the setting of MRLs for spices on the basis of monitoring data[40]. It was further clarified that chili peppers, herbs[41] and tea are excluded from the definition of spices, and GAP and corresponding supervised trial data should be used for estimation of maximum residue levels for these commodities.

The principal differences between the residue data derived from monitoring programmes and supervised field trials are as follows:

- The origin and treatment of the commodities sampled are not known.
- The sampled commodity might be aggregated from the produce of several small fields.
- The residues in spice samples are determined by multi-residue procedures with relatively high LOQs.
- When residue values are reported as being below the LOQ, it is not known whether the sampled commodity was or was not treated with or exposed to the pesticide.

[40] Report of the thirty-sixth session of the Codex Committee on Pesticide Residues, Alinorm 04/27/24, (paras 235 – 247) 2004, www.codexalimentarius.net

[41] Report of the thirty-seventh session of the Codex Committee on Pesticide Residues, Alinorm 05/28/24, (para 182) 2005, www.codexalimentarius.net

Consequently, estimation of maximum residue levels for pesticides on the basis of monitoring results requires a different approach to that used in evaluating the results of supervised residue trials.

The Meeting assumes that the Member States report only valid results. Therefore, all residue data are taken into account as there are no scientific grounds to exclude any value as an outlier.

The distributions of residues are scattered or skewed upwards, and no distribution fitting appeared to be appropriate. Consequently, distribution-free statistics should be used in estimating the maximum residue level, covering the 95th percentile of the population at the 95% confidence level. Thus, the estimated maximum residue level encompasses at least 95% of the residues with 95% probability (in 95% of cases). To satisfy this requirement, a minimum of 58–59 samples are required. The minimum sample size of 58 provides 95% assurance of finding at least one residue value above the 95th percentile of the residue population in the sampled object. It is not known, however, how many of the measured values are above the 95th percentile and what percentile (95.1th, 99th or 99.9th) the highest residue represents.

The procedure used for estimating maximum residue levels depends on the number of samples containing detectable residues.

- When no sample contains detectable residues, the highest reported LOQ value is used as the maximum residue level and the high residue value. The median residue value is calculated from the reported LOQ values.
- When large numbers of residue data is available, the highest residues may be above the upper confidence limit of the 95th percentile of the residues and they need not be considered in estimating maximum residue levels.
- Where the number of samples containing detectable residues does not allow the calculation of the upper 95th confidence limit for the 95th percentile, sufficient allowance should be given when the maximum residue level is estimated to be above the highest residue value observed. Note that the samples with residues reported below the LOQ cannot be taken into consideration as they were not necessarily treated with or exposed to the pesticide.

The 2004 JMPR recommended that monitoring results should not be used for estimating maximum residue levels that reflect post-harvest use, which results in much higher residue values than foliar application or spray drift exposure.

STMR and the highest residue values can be calculated only from supervised trials. The corresponding values from the monitoring data are indicated as median and high residue values, and these can be used like the STMR and highest residue values for estimating short-term and long-term dietary intake of residues (see Chapter **7**).

6.11.2 Estimation of extraneous maximum residue levels

Chemicals for which EMRLs (extraneous maximum residue limits) are most likely to be needed are those which have been widely used as pesticides, are persistent in the environment for relatively long periods after use has been discontinued and are expected to occur in foods or feeds at levels of sufficient concern to warrant monitoring.

Predictions of persistence in the environment (and the potential for uptake by food or feed crops) can often be based on a combination of data sources normally available for chemicals

previously approved as pesticides. These may include information on their physical and chemical properties, metabolism studies, data on supervised field trials, data on environmental fate, rotational crop data, the known persistence of similar chemicals, and especially from monitoring data.

All relevant and geographically representative monitoring data (including nil residue results) are required to make reasonable estimates to cover international trade. Better extraneous maximum residue level estimates, taking into account trade concerns, can be made when more extensive data are available. However, typically data are available from only three or four (usually developed) countries at the most. By the nature of national monitoring, data are usually received primarily on those commodities in which residues have been found at the national level and which have the potential to create trade difficulties.

In estimating an extraneous maximum residue level the JMPR attempts to take into account a number of factors. These include the amount of data, the relative importance of the commodity in international trade, the potential for trade difficulties or accounts thereof, the frequency of positive results, a knowledge of the propensity of a particular crop to take up residues, e.g., the uptake of DDT by carrots, historical monitoring data, e.g., previous monographs, and the level and frequency of residues in similar crops, especially those in the same crop group. In some cases the estimate has turned out to be the highest level reported, especially if a relatively good database is available and the spread of results is reasonably narrow.

In recent years there have been cases where the extraneous maximum residue level was estimated below the highest residue found, especially if the higher values occur infrequently. For example, the 1993 JMPR recommended an EMRL of 0.2 mg/kg for DDT in carrots, although 2 of 4 imported samples reported from one country were 0.4 and 0.5 mg/kg. The JMPR took into account that only 2 of over 800 imported samples exceeded 0.2 mg/kg. This limit covers > 99% of the residue population with 99% confidence. A similar approach was taken for DDT in the fat of meat by the 1996 JMPR. This approach also recognizes that residues gradually decline and that monitoring data can be outdated by the time they are received by the JMPR. It is more likely to be used when the higher residues occur infrequently.

In the context of EMRLs, the JMPR does not consider extreme values to be outliers in a statistical sense, because high residue levels are usually not true statistical outliers but values on one tail of a large distribution. The challenge is to decide when it is reasonable to discard those values in order to reflect the expected gradual decline in the levels of chemicals that are typically subject to EMRL recommendations, while not creating unnecessary barriers to trade.

Generally, the JMPR considers that the databases needed for estimating extraneous maximum residue levels should be substantial because the EMRL data are based on analysis of samples of unknown origin and very far from a normal distribution. (Note that it is difficult to compare the database required for EMRLs and MRLs because the nature of the data is quite different – supervised trials for MRLs and monitoring data for EMRLs). For example, samples from 598 randomly selected animals are needed to ensure that the estimated EMRLs cover 99.5% of a population, allowing a 0.5% violation rate with 95% confidence (Codex Alimentarius, Vol. II, 2nd Ed., p. 372). On the other hand, if a country had only 100 random samples analysed with a 10% violation rate this is quite significant, despite the small number of samples.

As EMRL databases are derived from the random monitoring of different populations, the JMPR does not normally consider a ‘world’ population of data, but gives independent consideration to different populations, e.g., of different geographical regions or of different

animals, before deciding which data populations might be combined. Therefore, all relevant monitoring data should be submitted regardless of the number of samples analysed.

The JMPR compares data distribution in terms of the likely percentages of violations that might occur if a given EMRL is proposed. Since there is no internationally agreed level of acceptable violation rate, the JMPR recommends EMRLs based on the available data. However, violation rates of 0.5 to 1% or greater are generally considered unacceptable.

The 2000 JMPR, in the evaluation of DDT in meat, estimated the residue levels in fat that related to violation rates of 0.1, 0.2 and 0.5%. The compromise among an acceptable violation rate, recommended EMRL and the potential for trade disruption are not scientific matters to be decided by JMPR. They are the province of risk manager decision making.

It is to be expected that there will be a gradual reduction or elimination of residues of the chemicals for which EMRLs have been proposed. The rate will depend on a number of factors, including the nature of the chemical, the crop, the location and environmental conditions.

Because residues gradually decrease, the JMPR recommends reassessment of EMRLs about every 5 years. Eventually, the data may indicate that there is no longer a need to monitor for the chemical. This view would be based on the conclusion that there is no longer a potential for significant disruption of trade and that the incidence or level of residues is no longer a significant health concern.

Although the JMPR does not use targeted monitoring data for estimating extraneous maximum residue levels, it agrees that follow-up studies are important when high residues are found in random monitoring to give a clearer view of the significance of the high levels. If properly conducted, such studies may indicate whether or not the higher residues resulted from intentional unauthorized uses and may allow the identification of areas in which production should be limited or where residue reduction strategies should be implemented.

6.12 ESTIMATION OF MAXIMUM RESIDUE LEVELS AND STMR VALUES FOR COMMODITIES OF ANIMAL ORIGIN

Residue levels in animal commodities, e.g. meat, milk and eggs, may arise from consumption of feed items containing residues or from direct application to a farm animal of a pesticide to control pests such as ectoparasites. Methods of estimating maximum residue levels in animal commodities have been developed in recent years and their detailed explanations were given in the JMPR reports.

The current procedures applied by the Meeting are described below.

6.12.1 Residues arising from consumption of feed items

Animals can be exposed, for extended periods, to certain commodities such as fodder, grain and feeds treated post-harvest containing residues at the highest level. In addition, in the experience of the Meeting, the residue levels of many pesticides on animal feed commodities show only a limited decrease during storage. Alternatively, it is unlikely that the individual ingredients of mixed feeds produced from commercially available ingredients would all contain residues at the theoretical maximum level.

Consequently, the highest residues in individual feed items are used for estimating the maximum residue levels in animal commodities, and the STMR or STMR-P should be applied to each of the components of mixed commodities. The STMR-P is also used for individual

feed items that are processed commodities, e.g., apple pomace. The estimation of residues that will arise in animal commodities is a two-step process involving farm animal feeding studies and dietary burden calculations. These two independent sets of information are compiled (Figure 6.5), then combined in order to estimate animal commodity residues that may arise.

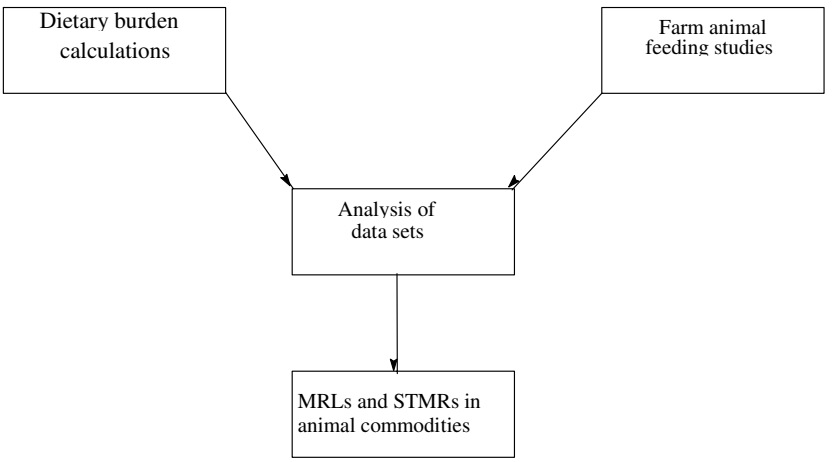

Figure 6.5 Estimation of residues in animal commodities

The following decision matrix is recommended for use in estimating maximum residue levels and STMR values:

Maximum residue level	STMR
Choose:	Choose:
feed commodity, highest residue or STMR-P (for dietary burden calculation)	feed commodity STMR or STMR-P (for dietary burden calculation)
highest residue level [a] (from feeding study in farm animals)	mean residue level[1] (from feeding study in farm animals)

STMR-P: supervised trials median residue in a processed commodity calculated by multiplying the STMR of the raw commodity by the corresponding processing factor

[a] Residue levels in tissues and eggs of the relevant group of animals in the feeding study. For milk, choose the mean residue in milk from the relevant group of animals in all cases.

The JMPR is currently utilising the livestock diets listed in the tables included in Appendix IX to estimate livestock dietary burdens from available residue data. To assists their use, Table IX.1 lists the Codex commodities with their code numbers corresponding to the feedstuffs. The tables IX.2-IX.4 include the Codex commodity group codes for all feedstuffs to facilitate the selection of commodities for calculation of the appropriate animal burden. The Excel spreadsheet which can be used for the calculations can be downloaded from the FAO/AGP Website (http://www.fao.org/ag/agp/agpp/pesticid/JMPR/.

The livestock diet tables were developed by the OECD Working Group on Pesticides[42]. They include data for beef cattle, dairy cattle, sheep, lambs, swine, broilers, layers and turkeys. Data are available from different geographic regions: Australia, Japan, EU, and US-Canada. Feedstuff categories in the OECD tables were chosen to ensure that the highest residue levels are estimated and a realistic although not nutritionally optimal livestock diet is composed. The

[42] http://www.oecd.org/document/52/0,2340,en_2649_34383_1897652_1_1_1_1,00.html

primary purpose of the tables was to estimate a highest livestock dietary burden from the geographic regions which could then be used to set an appropriate dosing regime for a livestock feeding study.

For simplicity and ease of use, the tables include information on percentage dry matter (DM) for each feed item as well as whether the STMR or highest residue (HR) should be used in the maximum dietary burden calculations. If the residues are already expressed on dry matter basis then the corresponding percentage of dry matter (DM%) should be replaced with 100%.

Feeding studies are normally available for lactating dairy cattle and laying hens. In such situations, livestock dietary burdens will be calculated for beef and dairy cattle, broiler and laying hens.

Maximum residue levels in animal commodities are derived from the highest residue values in feed commodities, and STMRs for animal commodities are derived from the STMRs for feed commodities. Separate tables are made for each MRL and STMR estimate, in which all feed items, their Codex commodity group and the residue levels found in crop residue trials are listed. The basis for the residue level is provided; i.e., the basis of the maximum residue level estimate is the highest level for raw agricultural commodities and the STMR-P for processed commodities.

The steps involved in the calculation are explained below with an example, see Table 6.3. For simplifying the example the Japanese feed consumption figures are not included, but should be considered in the evaluations.

a. The highest residue or the STMR /STMR-P values are entered into the Excel spreadsheet containing the corresponding livestock diet (Appendix IX), and the residues are expressed on dry weight basis;

b. The dietary burdens are calculated from commodity percent of diet;

c. Feed items having no residue value are deleted from the spreadsheet, and the remaining entries are sorted on Crop/Commodity group (ascending) and Residue DW (descending).

Table 6.3: Maximum dietary burden of beef cattle

Commodity/crop	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, dry	AB	0.038	STMR-P	100	0.038			*20*			0.01
Bean forage (green)	AL	2.1	high residue	35	6.000	*30*		*60*	1.80		3.60
Alfalfa fodder	AL	4	high residue	89	4.494	*60*		*80*	2.70		3.60
Pea vines (green)	AL	0.86	high residue	25	3.440	*20*	*20*	*60*	0.69	0.69	2.06
Maize fodder	AS AF	4.3	high residue	83	5.181	*25*	*25*	*40*	1.30	1.30	2.07
Wheat straw and fodder, Dry	AS AF	4.3	high residue	88	4.886	*10*	*20*	*80*	0.49	0.98	3.91
Barley forage	AS AF	1.4	high residue	30	4.667	*30*	*30*	*50*	1.40	1.40	2.33
Wheat milled (bran)	CM	0.084	STMR-P	88	0.095	*40*	*30*	*40*	0.04	0.03	0.04
Rice	GC	0.57	STMR	88	0.648	*20*		*40*	0.13		0.26
Wheat	GC	0.035	STMR	89	0.039	*20*	*40*	*80*	0.01	0.02	0.03
Total						*255*	*165*	*550*	8.54	4.40	17.91

d. Selection of commodities from each group

Starting with the feed item with the highest residue level, the percentage of each feed in the livestock diet is allocated. Usually, only one feed commodity from each Codex commodity group is used; if more than one is used, it is only up to the full percentage

feed allocation for that group. Note that some groups have two codes (e.g. AS and AF; AM and AV). Feeds are allocated a percentage of the diet for each animal until no more than 100% of the diet is used. The assignment of feed commodities to Codex groupds is illustrated in Figure 6.6

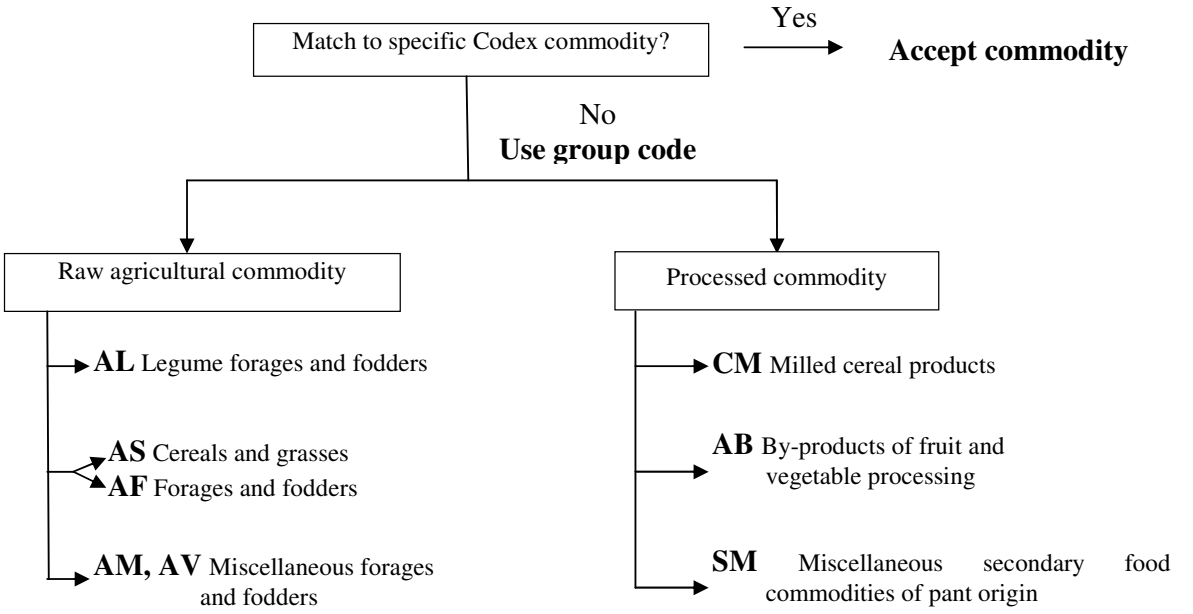

Figure 6.6 Grouping feed items for calculation of dietary burden of livestock

The first commodity group in Table 6.3 is AB, but with only one commodity, no change.

For AL (legume feeds) the animal diet content in US-Canada, Bean forage is first with 30%, no change. Alfalfa fodder is next with 60%, but bean forage has used 30% for the group, so alfalfa fodder becomes 30% (=60–30). As pea vines, at 20%, are less than the previous total for the group, the 20% is deleted.
For the animal diet content in EU, the only commodity is Pea vines with 20%, no change.

For the animal diet content in Australia, Bean forage is first with 60%, no change.
Alfalfa fodder is next with 80%, but bean forage has used 60% for the group, so alfalfa fodder becomes 20 % (=80–60). As pea vines, at 60%, are less than the previous total for the group, the 60% is deleted.

After selection of commodities within each group the following commodities remain (Table 6.4)

Table 6.4 Commodities selected to contribute to the maximum burden of beef cattle

Commodity/crop	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Grape pomace, dry	AB	0.038	STMR-P	100	0.038			*20*			0.01
Bean forage (green)	AL	2.1	high residue	35	6.000	*30*		*60*	1.80		3.60
Alfalfa fodder	AL	4	high residue	89	4.494	*30*		*20*	1.35		0.90
Pea vines (green)	AL	0.86	high residue	25	3.440		*20*			0.69	
Maize fodder	AS AF	4.3	high residue	83	5.181	*25*	*25*	*40*	1.30	1.30	2.07
Wheat straw and fodder, Dry	AS AF	4.3	high residue	88	4.886			*40*			1.95
Barley forage	AS AF	1.4	high residue	30	4.667	*5*	*5*		0.23	0.23	
Wheat milled (bran)	CM	0.084	STMR-P	88	0.095	*40*	*30*	*40*	0.04	0.03	0.04
Rice	GC	0.57	STMR	88	0.648	*20*		*40*	0.13		0.26
Wheat	GC	0.035	STMR	89	0.039		*40*	*40*		0.02	0.02
Total						*150*	*120*	*300*	4.84	2.26	8.85

e. If the total diet contributions exceed 100 % reduce diet contributions to 100 % in such a way as to retain the highest possible dietary burden. Delete (or reduce) the contributions from those commodities with lowest residue dw until the 100 % is achieved.

   Sort on Residue dw (descending), and delete the diet content values from the lower rows first, to achieve a 100% diet.

   For the US-Canadian list, delete the 40% for wheat bran, and reduce the rice to 10%. For the EU list, reduce the 40% wheat to 20% wheat. For the Australian list, retain only the first two entries to achieve 100% of diet (Table 6.5)

f. Where the selected feed items with residues from the use of the pesticide do not add up to 100% it is assumed that the animals are fed with other feed items which do not contain residue.

The STMR dietary burden is calculated from the STMR or STMR-P residue values estimated for the animal feed items following the same procedure as for the maximum burden.

Table 6.5 Selection of commodities to obtain 100% diet with maximum residue burden

Commodity/crop	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)* *US-CAN*	*EU*	*AU*	Residue contribution (ppm) US-CAN	EU	AU
Bean forage (green)	AL	2.1	high residue	35	6.000	*30*		*60*	1.80		3.60
Maize fodder	AS AF	4.3	high residue	83	5.181	*25*	*25*	*40*	1.30	1.30	2.07
Wheat straw and fodder, Dry	AS AF	4.3	high residue	88	4.886			~~*40*~~			
Barley forage	AS AF	1.4	high residue	30	4.667	*5*	*5*		0.23	0.23	0.00
Alfalfa fodder	AL	4	high residue	89	4.494	*30*		~~*20*~~	1.35		
Pea vines (green)	AL	0.86	high residue	25	3.440		*20*			0.69	
Rice	GC	0.57	STMR	88	0.648	***10***		~~*40*~~	0.06		
Wheat milled (bran)	CM	0.084	STMR-P	88	0.095	~~*40*~~	*30*	~~*40*~~		0.03	
Wheat	GC	0.035	STMR	89	0.039		***20***	~~*40*~~		0.01	
Grape pomace, dry	AB	0.038	STMR-P	100	0.038			~~*20*~~			
Total						*100*	*100*	*100*	*4.7416*	*2.2529*	*5.6724*

The calculation for dairy cattle and poultry are the same as for beef.

The final results of the calculated dietary burden as shown in Table 6.6 for beef-cattle, together with the dairy-cattle as well as broiler- and layer-poultry, are included as appendix of the Report of the JMPR.

Table 6.6: Final table with 100% diet calculation for maximum residue burden for beef cattle.

Commodity/crop	Commod group	Residue mg/kg	Basis	% Dry matter	Residue dw mg/kg	*Diet content (%)*			Residue contribution (ppm)		
						US-CAN	*EU*	*AU*	US-CAN	EU	AU
Bean forage (green)	AL	2.1	high residue	35	6.000	*30*		*60*	1.80		3.60
Maize fodder	AS AF	4.3	high residue	83	5.181	*25*	*25*	*40*	1.30	1.30	2.07
Barley forage	AS AF	1.4	high residue	30	4.667	*5*	*5*		0.23	0.23	
Alfalfa fodder	AL	4	high residue	89	4.494	*30*			1.35		
Pea vines (green)	AL	0.86	high residue	25	3.440		*20*			0.69	
Rice	GC	0.57	STMR	88	0.648	*10*			0.06		
Wheat milled (bran)	CM	0.084	STMR-P	88	0.095		*30*			0.028	
Wheat	GC	0.035	STMR	89	0.039		*20*			0.008	
Total						*100*	*100*	*100*	*4.74*	*2.25*	*5.67*

The maximum and STMR dietary burdens used for the estimation of maximum and STMR residues are reported in the appraisal of the evaluation of residues (Table 6.7).

Table 6.7: Example for summarising the maximum and STMR livestock dietary burdens

	Livestock dietary burden, [xxxx compound], ppm of dry matter diet					
	US-Canada		EU		Australia	
	max.	mean	max.	mean	max.	mean
Beef cattle	4.74	2.83	2.25	2.03	5.67	4.05
Dairy cattle	4.55	3.1	4.79	3.27	6.12[a]	4.07[b]

[a] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian tissues and milk
[b] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian tissues and milk.
Note: if the maximum or mean burden for beef is higher than that of dairy cattle then those values shall be used for estimation of residue levels for mammalian tissues.

6.12.1.1 Use of the calculated dietary burdens to estimate maximum residue levels and STMR values for commodities of animal origin

The calculations of dietary burden are compared with the feeding levels in studies of farm animals to estimate maximum residue levels and STMR values on the basis of the following guidelines.

- When a feeding level in a feeding study matches the dietary burden, the residue levels reported in the study can be used directly as estimates of residue levels in tissues, milk and eggs resulting from the dietary burden.
- When a feeding levels in a feeding study differs from the dietary burden, the resulting residues in tissues, milk and eggs can be estimated either by interpolation between the closest feeding levels or calculation from the linear regression equation if good fit is observed as shown in Figure 6.7.
- When the dietary burden is below the lowest feeding level in the study, the resulting residues in tissues, milk and eggs can be estimated by applying the transfer factor (residue level in milk or tissue ÷ residue level in diet) at the lowest feeding level to the dietary burden.
- When the dietary burdens of beef and dairy cattle are different, the higher value should be used for calculating the residues in muscle, fat, liver and kidney, as in the case shown in Table 6.7.

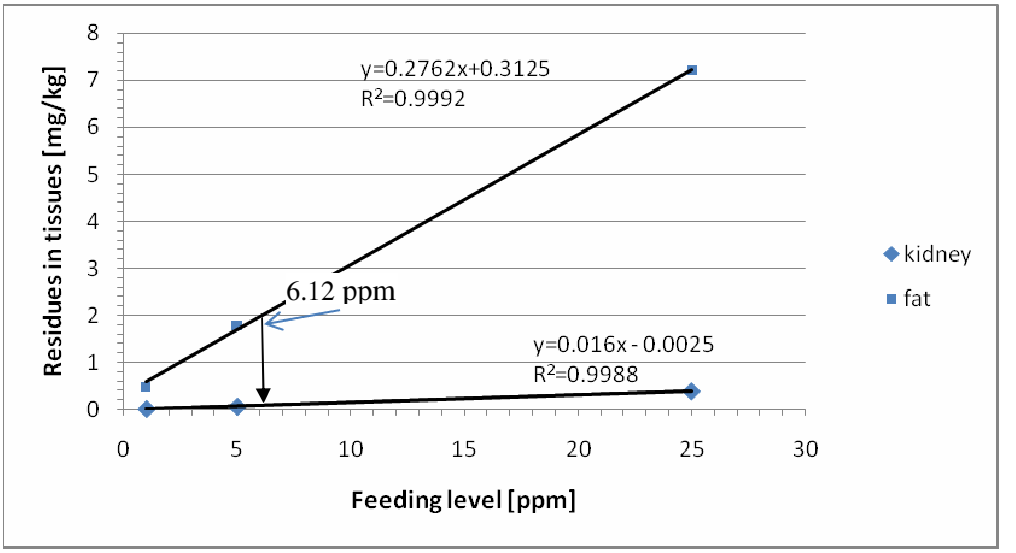

Figure 6.7 Interpolation between closest feeding levels

- For estimating maximum and highest residue levels in meat, fat, liver, kidney and eggs, the highest residue level found in an animal in the relevant feeding group of the study should be used.
- For estimating STMR values in meat, fat, liver, kidney and eggs, the mean residue levels in animals in the relevant feeding group of the study are used.
- For estimating maximum residue levels and STMRs in milk, the mean residue levels in the animals in the relevant feeding group of the study are used.
- No more than about 30% above the highest feeding level can be extrapolated to a dietary burden.

The estimated maximum and mean animal dietary burdens (listed in Table 6.7) are compared with the residues obtained from animal transfer studies for estimating maximum residue levels and STMR for animal commodities.

For MRL estimation, the high residues in the tissues are calculated by interpolating the maximum dietary burden (6.12 ppm) between the relevant feeding levels (5 and 25 ppm) from the dairy cow feeding study and using the highest tissue concentrations from individual animals within those feeding groups.

The STMR values for the tissues were calculated by interpolating the mean dietary burden (4.07 ppm) between the relevant feeding levels (1 and 5 ppm) and using the mean tissue concentration from each feeding group.

In Table 6.8 below, dietary burdens are shown in round brackets (), feeding levels and residue concentrations from the feeding studies are shown in square brackets [] and estimated concentrations related to the dietary burden are shown without brackets.

The data from the dairy cattle feeding study are used to support mammalian meat and milk MRLs, as the dietary burden for dairy cattle is higher than that of beef-cattle.

The mean and highest residues corresponding to the calculated maximum and mean dietary burden are used for estimation of maximum residue levels and STMR values for the relevant animal commodities taking into account the fat solubility of the residues.

Table 6.8 Summary of residues corresponding to the estimated dietary burden

Dietary burden (ppm) Feeding level [ppm]	Milk	Muscle	Liver	Kidney	Fat
MRL					
	mean	highest	highest	highest	highest
MRL beef or dairy cattle (6.12) [5, 25]	0.12 [0.1, 0.57]	0.1 [0.07, 0.4]	0.02 [0.01, 0.08]	0.09 [0.07, 0.4]	2.2 [1.8, 7.2]
STMR					
	mean	mean	mean	mean	mean
STMR beef or dairy cattle (4.07) [1, 5]	0.08 [0.03, 0.1]	0.04 [0.01, 0.05]	0.008 [0.03, 0.01]	0.03 [0.01, 0.04]	1.0 [0.25, 1.3]

Where the pesticide also has veterinary uses and JECFA has recommended maximum residue limits for animal commodities the higher residues deriving from the two kinds of use will form the basis for recommending maximum residue levels for Codex purposes.

6.12.2 Residues arising from direct application to farm animals

Pesticides may be applied directly to farm animals for control of lice, flies, mites and ticks. Application methods include dips, sprays, pour-ons and jetting. Residue trials using the required method of application, dosage and withdrawal times are needed if residues may occur in animal commodities.

The number of supervised trials on animals is, of necessity, far less than for crops. (See also Chapter 3 Section 9 "*Information and data from farm animal feeding and external animal treatment studies*".

The conditions of a supervised residue trial on farm animals should match the maximum conditions described on the label. If more than one application method is permitted, e.g., dip or pour-on treatments, residue data should be available for each method. The evaluation should record the highest residue occurring in individual animal tissues resulting from the approved method and dose. The highest residues will support the MRL recommendations. The evaluation should record the average milk residues each day across the treatment group and the MRL recommendation will depend on the highest of these average milk residues on a day achieved within the conditions described on the label.

The STMR concept is designed for supervised field trials on crops to obtain the typical residue value when a pesticide is used at maximum GAP. The STMR methodology is not directly applicable to a single direct-animal treatment trial. However, the idea of a typical residue value when a pesticide is used directly on animals (at maximum label conditions) is useful in long-term dietary intake estimations. For this purpose the median of the residues in the tissues of animals slaughtered at the shortest interval after treatment (or later if residues were higher later) is taken to represent that typical value.

6.12.3 Reconciliation of MRL recommendations resulting from direct treatment and from residues in animal feed

Where the maximum residue level recommendations from the two sources of residues do not agree, the higher recommendation will prevail. Similarly, the estimates for typical residues

from direct use at maximum label conditions or STMR values derived from the farm animal dietary burden and animal feeding studies, whichever is the higher, should be adopted for long-term intake estimation.

6.13 EXPRESSION OF MAXIMUM RESIDUE LIMITS (MRLs)

The estimated maximum residue levels and recommended residue limits are expressed in mg residue (as defined)/kg commodity. The portion of commodity to which Codex MRLs apply is given in Codex Alimentarius Vol. 2 (extracted in Appendix VI).

The residues are expressed on fresh-weight basis or as they enter international trade (as received by the laboratory) in most commodities, with the exception of animal feeds. Because of the great variation of their moisture content, MRLs for animal feeds are recommended on a dry-weight basis. This implies that the commodity is analysed for pesticide residues as received, that the moisture content of the sample is determined (preferably) by a standard method recommended for use on that commodity, and that the residue content is then calculated as if it were wholly contained in the dry matter.

If it is not clear in animal feed residue data submissions whether residues are expressed on a dry weight basis, or the moisture content of the feed is not reported, either a 'worst case' assumption could be made that the residues are expresses on a fresh weight basis or the data may not be suitable for estimating maximum residue levels.

For animal products there are certain special cases which need to be mentioned:

For meat and fat-soluble pesticides (see also Chapter 5 section 2 "*Physical and chemical properties*" and Chapter 3 section 9.3.1 "*Nature of fat samples in studies on fat-soluble compounds*") the residue limits for meat are expressed on the fat (the residue content in trimmable fat or fat tissue expressed on the lipid content) which is indicated in brackets (fat) after the residue value. For those commodities where the adhering fat is insufficient to provide a suitable sample, the whole meat commodity (without bone) is analysed and the MRL applies to the whole commodity.

For all other pesticides the MRLs apply to the whole commodity as it moves in trade.

During the past years, the MRLs and EMRLs for fat-soluble pesticide residues in milk and milk products had been expressed on a calculated whole product basis assuming all milks to contain 4% fat. Milk products with a fat content of 2% or more had been expressed on a fat basis. The MRL would be 25 times the MRL for milk, i.e., the same value as if expressed on the fat of milk. The MRL for milk products, with a fat content lower than 2%, were considered to be half the value for milk and are expressed on a whole product basis.

The 2004 JMPR decided that two maximum residue levels would be estimated, if the data permit: one for whole milk and one for milk fat. For enforcement purposes, a comparison can be made either of the residue in milk fat with the MRL for milk (fat) or of the residue in whole milk with the MRL for milk. When needed, maximum residue levels for milk products can then be calculated from the two values, by taking into account the fat content of the milk product and the contribution from the non-fat fraction.

Milk MRLs for fat-soluble pesticides were indicated by the letter "F".

Examples for recommended MRLs (mg/kg) for diazinon –

MO 0098	Kidney of cattle, pigs and sheep:	0.03
MM 0097	Meat of cattle, pigs and sheep:	2 (fat)
ML 0106	Milks	0.02 F

Based on the decision of the 2008 CCPR, a footnote will be inserted to indicate where MRLs are established for both milk fat and whole milk: "for monitoring and regulatory purposes, whole milk is to be analysed and the result compared to the MRL for whole milk".

For compounds that are not fat-soluble, MRLs are expressed on the whole milk.

MRLs based on direct animal treatment are footnoted "the MRL accommodates external animal treatment".

MRLs reflecting special uses or conditions are also distinguished by letters after the limit: Currently the following cases are distinguished by the letters indicated below:

E	The MRL is based on extraneous residues
Po	The MRL accommodates post-harvest treatment of the commodity
PoP	The MRL for the processed commodity accommodates post-harvest treatment of the primary commodity

In order to more fully reflect the impact of the statistical calculation methods, the JMPR concluded that the scaling steps last presented in the 2001 JMPR Report (0.01, 0.02, 0.03, 0.05, 0.07, 0.1, 0.2, 0.3, 0.5, 0.7, 1, 2, 3, 5, 7, 10, 15, 20, 25, 30, 40, and 50 mg/kg would be replaced with a more detailed scale where the statistical tools are successfully used. The Meeting continues using one significant figure for residues below 10 mg/kg and 2 significant figures up to 99 mg/kg. Residues from 100 would be expressed as multiple of 10, e.g., 110, 120. Applying more digits in expressing the MRLs would provide a false impression on the precision (uncertainty) of the estimation process including also the uncertainty of sampling, sample preparation and analysis. Nevertheless, the option to use other values as necessary is maintained.

6.13.1 Expression of MRLs at or about the LOQ

The LOQ is the lowest concentration of a compound that can be determined in a commodity with an acceptable degree of certainty. See Appendix II "Glossary of terms".

The JMPR recognizes the difficulties that may arise in regulatory laboratories analysing low levels of residues in samples of unknown origin, and so usually estimates an LOQ which is achievable under those conditions. It is this figure that is proposed as a maximum residue limit "at or about the LOQ". These limits are indicated with an asterisk (*) after the numerical value, e.g., 0.02*. This limit is often referred to as a "practical LOQ" to distinguish it from the LOQs reported in supervised trials.

An MRL so identified does not always necessarily imply that residues of the pesticides do not occur in that commodity. The application of a more sensitive or specific method may reveal detectable residues in some commodities as shown, e.g., in Tables 14 and 26 of the 1995 monograph on quintozene[43].

In many instances the use of a pesticide according to GAP results in a residue level in crops or commodities that is too low to be measurable by available analytical methods. Setting and enforcing MRLs for residues occurring at or about the LOQ of analytical procedures may require different approaches depending on the composition and definition of the residues. It is emphasized that all available relevant information should be carefully considered ensuring

[43] Pesticide residues in food—1995 evaluations. Part I. Residues. FAO Plant Production and Protection Paper 137, 1996.

that an MRL established at a level equivalent to a practical LOQ of the individual residue components will fully accommodate the levels of these components which could occur in commodities following treatment according to GAP.

As in cases of detectable residues, the definition of residues at or about the LOQ may also include a single residue component, e.g., fenpropimorph in sugar beet, or several residues components, e.g., aldicarb, its sulphoxide and its sulphone expressed as aldicarb in peanut oil, bentazone, 6-hydroxy bentazone and 8-hydroxy bentazone expressed as bentazone in soya bean; and fenthion, its oxygen analogue and their sulphoxides and sulphones expressed as fenthion in potato.

In cases where several metabolites are included in the definition of the residue two basic situations can be distinguished.

a. The residue components are, or may be converted to, a single compound or analyte by the analytical method, e.g., fenthion. The total residue is measured as a single compound and expressed as the parent compound, i.e., fenthion oxygen analogue sulphone is measured and expressed as fenthion. The MRL is set and enforced on the basis of the total measured residue. After the conversion of all the residue components a single compound is determined, the MRL can be simply enforced either at or above the LOQ. This situation is similar to other cases where the residue is defined as a single compound.

b. The residue components are determined separately by the method. The concentrations of measurable residues are adjusted for molecular weight and summed, and their sum is used for estimating the maximum residue level.

The problem is best illustrated with an example. The residues of bentazone in plant commodities are defined as the sum of bentazone, 6-hydroxybentazone and 8-hydroxybentazone, expressed as bentazone. The LOQs reported in supervised trials for each of the three components were generally 0.02 mg/kg, but the practical LOQs were regarded as 0.05 mg/kg for regulatory purposes. If an MRL for bentazone was set as the sum of the practical LOQs of the three components of the residue, it would have to be established at 0.2 mg/kg (3 times the practical limit of determination to incorporate all three residue components and round it to the next whole number). In this case, any one of the residue components could be present at 0.2 mg/kg, or all of the three at 0.06 mg/kg, without exceeding the MRL. Consequently, individual residue components could be respectively 10 and 3 times those which should arise from the recommended use of the compound but would be within the MRL. Similarly, if the sum of the LOQs achieved in the supervised trials was considered, an MRL of 0.1 mg/kg would be needed, which would still allow 5 times the residue that would arise from treatments complying with GAP.

The 1995 JMPR concluded that when residues are undetectable in a commodity an MRL based on the sum of the LOQs of the individual residue components may not be appropriate for enforcement purposes. The best option should be selected on a case-by case basis taking into account the relative ratio of metabolites.

From the regulatory laboratory perspective the best option is to choose a simple enforcement residue definition, i.e., a single component if possible. Standards of the single component should be readily available and not excessively expensive.

6.14 RECOMMENDATIONS FOR MAXIMUM RESIDUE LIMITS

The JMPR recommends to the CCPR that the estimated maximum residue levels be used as MRLs if the risk assessment process demonstrates that consumption of the relevant foods does not result in dietary intakes of residues exceeding the ADI or ARfD (Chapter 7, "*Estimating dietary intake of pesticide residues*").

In those cases where a full ADI could not be estimated or the previously estimated ADI has to be withdrawn, the JMPR does not recommend MRLs or withdraws its previous recommendation

6.14.1 Recommendation of temporary MRLs

A temporary maximum residue limit is a maximum residue limit for a specified limited period, which is clearly related to required information.

As a general JMPR policy, TMRLs will not be introduced for a new compound, a compound in the periodic review programme or when there is no established GAP.

In the past the JMPR recommended a TMRL in some special circumstances on a case-by-case basis, for example:

- The JMPR was informed that experiments were in progress and data from residue or processing trials would be available for a specified meeting in the future.
- Immediate withdrawal of an MRL might be too disruptive if insufficient opportunity had been given for comment and data submission.
- TMRLs for specific commodities were recommended to replace group commodity MRLs or "fruit" and "vegetable" MRLs where residue trials on those specific commodities were known to be in progress

6.14.2 Guideline Levels

A Guideline Level is the maximum concentration of a pesticide residue occurring after use of the pesticide according to Good Agricultural Practice, but for which no Acceptable Daily Intake has been established or it has been withdrawn by the JMPR. There may still be a need to inform regulatory authorities about the residue levels to be expected in food items when these pesticides are used in accordance with Good Agricultural Practice.

Over a number of years the Codex Committee established a list of Guideline Levels for pesticides. These Guideline Levels had not been submitted to the Commission for adoption, but were used for the internal reference of the Committee. In 1993 the Codex Alimentarius Commission decided that Guideline Levels would no longer be established. The existing Guideline Levels had been submitted to a review programme in order to delete compounds from the list. Currently, Guideline Levels exist for methyl bromide and guazatine.